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A JOURNAL FOR THE STUDY OF THE CIRCULATION

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UNDER THE EDITORIAL DIRECTION OF

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Original Communications

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The American Heart Journal

VOL. 14 JULY, 1937 No. 1

Original Communications

SOME REMARKS ON THE TECHNIQUE IN CLINICAL ELECTROCARDIOGRAPHY WITH PRECORDIAL DERIVATION*

KAJ H. LARSEN, M.D.
COPENHAGEN, DENMARK

AMONG other properties the following have contributed to the hitherto prevailing employment of derivations from the extremities in clinical electrocardiography: 1. The relatively uniform appearance of these derivatives in normal persons, e.g., the P- and T-waves are always positive in Leads I and II. 2. Their constant form on repeated examinations of the same person, owing to the fact that even considerable changes in the localization of the electrodes on the extremities and in the position of the subject give but very slight changes in the form of the curves.

In the choice of precordial derivations for routine employment it will be expedient to select leads that have the same properties as far as possible.

The precordial derivations now employed are all "semidirect" (Wilson and associates[11]) or "unipolar" (Groedel[3]), meaning that one electrode (the principal) is placed on the precordium (just over the heart or in its immediate vicinity), while the other electrode (the indifferent) is placed so far away from the heart that the variations of potential at that point are very small in proportion to the variations on the principal electrode. The ideal would be an indifferent electrode with the potential constantly = 0. But the human body has no region where every individual shows complete absence of potential variations due to the heart action. Nor is an ideal zero electrode obtainable after the method given by Wilson and collaborators[12] or by Storti.[10]

The significance of the location of the indifferent electrode to the form of the electrocardiogram is evident from Figure 1, which shows different precordial derivations in a man, aged twenty-one years, with-

*From the University Medical Clinic B, Rigshospital, Copenhagen. (Chief: Professor E. Warburg, M.D.)

out any circulatory disturbance. All the electrocardiograms are taken with the amplifier electrocardiograph described earlier by Larsen.[5] Each picture shows two derivations taken at the same time. No change whatever was made in the location of the *principal* electrode, while the place of the *indifferent* electrode was varied as recorded in the legend of the figure. It will be noticed that the P- and T-waves in both derivations are distinctly positive when the indifferent electrode is placed on the right arm, while this is not the case with the other localizations. (In *B*, Td is "humpy," in *C*, Ps is isoelectric, in *E*, Td is "humpy," and in *F*, Pd and Ps are diphasic, Td, negative.) Examination of five other normal subjects showed similar conditions. If we wish to employ only one localization of the indifferent electrode, it will therefore, according to the view set forth in the introduction, appear to be most expedient to choose the electrode of the right arm for indifferent electrode. It has been my experience with a few hundred normal adults that, with this localization of the indifferent electrode, the P- and T-waves always are positive—at any rate with the given localizations of the principal electrode. That other localizations of the in-

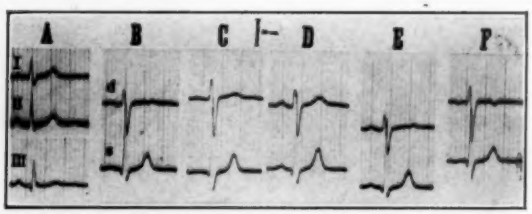

Fig. 1.—Derivations from the extremities and various semidirect precordial derivations in a man aged twenty-one years, without circulatory disturbances.

A: Derivations from the extremities.

B-F: Precordial derivations. In derivation *d* the different electrode was placed every time at the lower left corner of the sternum, in derivation *s* it was placed every time with its center 4 cm. lateral to, and at a level with, the apex of the heart. The indifferent electrode in *B* was Wilson's electrode,* in *C* it was an electrode at the angle of the right scapula, in *D* it was the electrode on the right arm, in *E*, the electrode on the left arm, and in *F*, the electrode on the left leg.

Timer = 0.05 sec. 1 millivolt = ca. 20 mm. in the original.

different electrode give a more variable form to the P- and T-waves is also evident from the studies on normal adults reported by Goldbloom,[2] Katz and Kissin,[4] Master,[7] and Shipley and Hallaran.[9] To use the right-arm electrode for indifferent electrode also offers the advantage that the deflections become greater in this way than with any other localization of the indifferent electrode (Einthoven and de Lint,[1] Roth,[8] the writer's own experience).

As to the localization of the principal electrode it may be said generally that larger waves are obtained by derivation from the precordium proper than by derivation a little outside the heart borders, and that a displacement of the electrode in the former location gives

*Wilson's[12] electrode is formed by joining the electrodes on the right arm, left arm, and left leg through resistances of 5,000 ohms (in our clinic 10,000 ohms) and using this junction for indifferent electrode.

greater changes in the form of the electrocardiograms than does an equal linear displacement of the electrode in the latter place. The last point is illustrated plainly in Figure 2 (note legend); examination of two other persons showed similar conditions. So it is to be

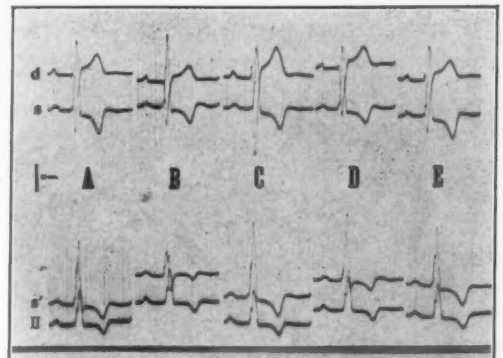

Fig. 2.

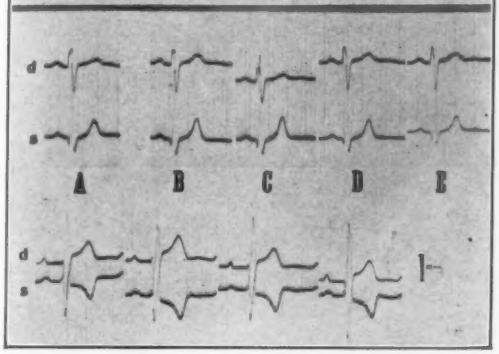

Fig. 3.

Fig. 2.—Precordial derivations from a man, aged thirty-five years, with rheumatic aortic disease.

In *A* the principal electrode in Lead *d* was placed at the lower left corner of the sternum, in Lead *s* its center was localized 4 cm. lateral to, and at a level with, the apex of the heart, in Lead *s'* it was placed over the apex of the heart. The electrode on the right arm served as indifferent electrode. In the following records (*B-E*) the electrodes are shifted (electrode *d:* 1.5 cm. electrodes *s* and *s':* 3 cm.) respectively to the right in *B*, to the left in *C*, upwards in *D*, and downwards in *E*.

In this way, Lead *s'* shows greater variations than Lead *s*.

Timer = 0.05 sec. 1 millivolt = ca. 20 mm. in the original.

SIZE OF THE MORE IMPORTANT WAVES IN FIGURE 2, IN MM.

	LOCALIZATION OF ELECTRODES	RD	SD	TD	RS	SS	TS	RS'	SS'	TS'
A.	d: Lower left sternal angle s: 4 cm. lateral to apex of heart s': Apex of heart	1.3	— 42.0	15.3	51.8	— 0	— 16.8	49.0	— 4.6	10.0
B.	Shift to right	0.5	32.0	11.2	53.0	sug-gest.	12.6	19.5	10.0	2.8
C.	Shift to left	9.0	57.5	23.0	45.5	0	14.7	57.0	sug-gest.	14.2
D.	Shift upwards	1.5	35.5	15.0	46.0	sug-gest.	10.7	49.0	5.8	7.8
E.	Shift downwards	4.4	38.0	13.3	50.6	0	17.0	43.0	2.8	13.0

Fig. 3.—The upper row shows the precordial derivations *d* and *s* in a man, aged twenty-one years, without circulatory disturbances, the lower row shows the same derivations in a man aged thirty-five years, with rheumatic aortic disease.

In *A* the subject is lying on his back (ordinary posture), in *B* he is half lying on his right side, *C*, half lying on his left side, *D*, half sitting, *E*, sitting.

Timer = 0.05 sec. 1 millivolt = ca. 20 mm. in the original.

pointed out that derivation from a place a little lateral to the apex of the heart implies a greater possibility of uniformity of the curves, on repeated examinations, than may be obtained with derivation from the apex of the heart.

The localizations most commonly employed for the principal electrode are the apex of the heart and the left fourth intercostal space, just at the border of the sternum. The writer employs the derivations given by Groedel,[3] namely: from the lower left corner of the sternum to the right arm (Lead *d*), and from a point (i.e., the center of the electrode) 4 cm. lateral to, and at a level with, the apex of the heart to the right arm (Lead *s*). Groedel takes his derivations to present potential variations in relation to the variations of potential in the right and left ventricles, respectively. Figure 3 illustrates how little the form of the electrocardiograms with these derivations is influenced by differences in the positions of the subjects (note legend). Forced breathing

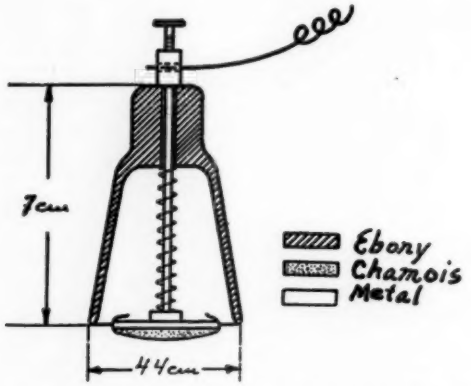

Fig. 4.—Electrode for the taking of precordial derivations.

and slow deep breathing gave no particular changes in the curves. For particular study of the P-wave (block and auricular fibrillation) the writer uses a derivation from the right third intercostal space, just at the sternal margin, to the right arm.

In routine electrocardiography with precordial derivations, the electrode depicted in Figure 4 has been of great help to us. After the derivations from the extremities are taken in the usual manner, the left-arm lead of the electrocardiograph is fastened—in keeping with the rule formulated by Larsen and Warburg[6]—to the precordial electrode, and the desired precordial derivation is taken as Lead I. The method requires an assistant to hold the electrode firmly against the given spot on the thorax—but anybody present may serve as assistant. The diameter of the metal plate is 3 cm. There will hardly be any reason to use electrodes of smaller diameters; besides, smaller diameters would also make it more difficult to make the curves look alike on repeated examinations, for it is found that, with equal linear displace-

ment of a large electrode and a small one (i.e., displacement of their centers), the smaller electrode gives greater changes in the form of the curves than does the large electrode. An example of this is shown in Figure 5 (note legend), and the same was found on examination of two other persons.

SUMMARY

The most favorable localization of the indifferent electrode in semi-direct precordial derivations is the right arm, because this localization gives a more uniform appearance of the electrocardiograms of normal adults and greater deflections than other localizations of the indifferent electrode.

It is shown that the form of the precordial derivations *d* and *s* given by Groedel is only little changed by minor variations in the position of the patient and in the localization of the electrodes.

A handy electrode for the routine taking of precordial derivations is shown, and the effects of variations in the size of the electrode are demonstrated.

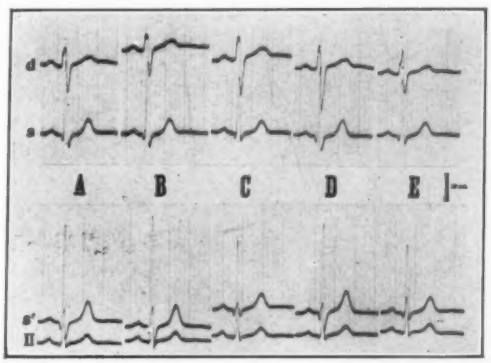

Fig. 5.—Precordial electrocardiograms from a man, aged twenty-one years, without circulatory disturbances.

Upper row: *A* gives the derivations *d* and *s*. In the following pictures (*B*-*E*) the centers of the electrodes have been shifted—electrode *d*, 1.5 cm., electrode *s*, 3 cm., respectively, to the right in *B*, to the left in *C*, upwards in *D*, and downwards in *E*. An electrode of 6 cm. in diameter was used in taking derivation *s*.

Lower row: An electrode of 3 cm. is used in taking derivation *s'*, the center of this electrode being placed on the points where the center of electrode *s* was placed in taking the upper row.

On comparison of derivations *s* and *s'*, the variations on the size of the waves are seen to the greatest in derivation *s'*.

Timer = 0.05 sec. 1 millivolt = ca. 20 mm. in the original.

SIZE OF THE MORE IMPORTANT WAVES IN FIGURE 5, IN MM.

LOCALIZATION OF ELECTRODES	RD	SD	TD	RS	SS	TS	RS'	SS'	TS'
d: Lower left sternal angle		—			—			—	
A. s: 4 cm. lateral to apex of heart	13	18.5	6.3	56.0	9.5	12	73.5	12.0	16
s': 4 cm. lateral to apex of heart									
B. Shift to right	11	19.0	7.0	55.0	8.5	12	84.0	13.0	17
C. Shift to left	16	27.0	8.0	43.0	5.0	10	53.0	4.5	12
D. Shift upwards	18	31.5	6.0	53.5	9.0	12	68.0	11.5	16
E. Shift downwards	17	14.5	8.0	43.0	6.0	10	52.0	5.5	12

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A RATIONAL PRINCIPLE FOR THE CONNECTIONS OF THE LEADS OF THE ELECTROCARDIOGRAPH IN CLINICAL ELECTROCARDIOGRAPHY WITH PRECORDIAL DERIVATION*

KAJ H. LARSEN, M.D., AND ERIK J. WARBURG, M.D.
COPENHAGEN, DENMARK

SINCE Wolferth and Wood[16, 17, 18, 19] in 1932 and 1933 reported their employment of precordial derivations in clinical electrocardiography, this question has attracted considerable interest, as is evident from a great number of papers from all parts of the world. Under the circumstances therefore it is highly desirable that a uniform technique for the taking of precordial electrocardiograms should be adopted in order that tracings everywhere may be standardized and comparable.

Wolferth and Wood connect the lead of the electrocardiograph for the right arm to the principal electrode (nearest the heart), and the lead for the left leg to the indifferent (remote) electrode; with such a connection, the T-wave in normal adults is inverted, and hence the electrocardiogram will look like a mirror image when compared with the leads from the extremities. A great many investigators have employed this connection of the leads, e.g., Goldbloom,[3] Hoffman and Delong,[5] Katz and Kissin,[7] Levy and Bruenn,[9] Master,[11] Rosenblum and Sampson,[12] Shipley and Hallaran,[14] and Wilson and his associates.[15] Others have found it more practical and in principle more proper to have the normal T-wave recorded in the same direction in precordial derivations as in derivations from the extremities, and hence they have arranged the leads reversely, i.e., have connected the lead for the right arm to the indifferent electrode and the lead for the left arm or left leg to the precordial electrode—as is done, among others, by Groedel,[4] Jervell,[6] Liberson and Liberson,[10] and Roth.[13] No doubt, one can accustom oneself to normal negative T-waves (i.e., downward deflections of the curve) as well as to normal positive T-waves, but it takes a very considerable training in reading electrocardiograms as fast and correctly as usual, if they are taken now in one way, then in another. Moreover, as long as there is no established rule for this procedure, one must always have information about the connection of the leads.

As is well known, Einthoven[1, 2] followed the rule that the connection of the leads, the polarity of the galvanometer, and the direction of the

*From the University Medical Clinic B, Rigshospital, Copenhagen. (Chief: Professor E. Warburg, M.D.)

movement of the photographic film shall agree mutually in such a way that a negative potential impressed upon the right-hand or cranial electrode is registered on the curve as an upward deflection, when the curve is read from the start (at the left) toward the right. This principle is not directly applicable to precordial derivations, however, for then a negative potential impressed on the precordial electrode will be registered as an upward deflection of the curve if the indifferent electrode is localized to the left or caudally to the precordium (for example on the left leg), but as a downward wave if the indifferent electrode is localized to the right or cranially to the precordium (e.g., on the right arm). As it is agreed in general that the variations of potential at the precordial electrode are so great in proportion to the variations of potential at the indifferent electrode as to determine in all essentials the appearance of the precordial electrocardiogram, it seems irrational that this dominating potential in some precordial derivations is registered as an upward wave on the curve, in others as a downward wave. On the other hand, it would be a rational thing to adopt the following rule:

The connection of the leads, the polarity of the galvanometer and the direction of the movement of the photographic film are to agree mutually in such a way that a negative potential impressed on the (chest) electrode is recorded on the curve as a downward deflection, the curve being read from the start (at left) toward the right.

This is in keeping with the general principles of graphic recording. This rule is observed if, on an ordinary electrocardiogram, the lead for the right arm is connected to the indifferent electrode, while one of the other leads is connected to the principal electrode.

The leads employed by Wolferth and Wood are contrary to the above rule, as an upward deflection of the curve in their electrocardiogram means that the precordial electrode has been negative in relation to the indifferent electrode. Wolferth and Wood adopted this method because they wanted the greatest possible similarity between their curves from patients with infarction of the heart and their curves from animals with experimental infarcts, and in their introductory animal experiments, for no given reasons, these investigators had connected the lead for the right arm to the principal electrode.

By following the rule enunciated above we get precordial electrocardiograms to which the nomenclature given by Einthoven,[1] and now employed everywhere, is directly applicable; whereas this is associated with some difficulties in precordial electrocardiograms taken with the opposite connection of the leads. After Einthoven, the first wave in the initial complex is designated as Q if it points downward, and as R if it points upward, while a downward wave that comes after an upward is designated as S, as S is also designated the downward wave

in cases when there is no upward wave at all. In normal persons, as is well known, R is the most constant and highest wave in the initial complex in derivations from the extremities.

That this is the case also in many precordial leads taken according to the rule given above, is evident from illustrations presented in a paper on precordial leads by Kaj H. Larsen.[8] If the electrocardiograms shown in these pictures had been taken with the opposite connection of the leads, the most constant and greatest wave in the initial complex would have pointed downward, and then it would have to be designated, after Einthoven, as Q or S, depending on whether or not it was preceded by an upward wave. But to designate this constant wave as Q or S must be said to be irrational, as in reality it is an R-wave, being synchronous with the R-waves in derivations from the extremities. This is seen in synchronous electrocardiograms taken with precordial derivation and with derivation from the extremities as shown, for example, in the aforementioned paper by Kaj H. Larsen, Fig. 5, lower row.

SUMMARY

A hard and fast rule for the making of precordial electrocardiograms has been given which insures that the direction of the waves will be in conformity with the rules generally applied to the registration of events in the standard leads.

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HEART MURMURS

From the Viewpoint of an Actuary

Arthur Hunter, LL.D.
New York, N. Y.

RECENTLY I had occasion to review the medical literature on the subject of heart murmurs, with especial regard to the effect on longevity. To my surprise I was unable to find any comparison made by a heart specialist of the death rates among persons with heart murmurs in relation to the normal mortality, i.e., no statement had appeared of the extra mortality based on experience. Moreover, I did not see any reference to the extensive investigations made by the life insurance companies, through the cooperation of their medical directors and actuaries. The purpose of this article is to give the medical profession a synopsis of the mortality experiences of these companies, prepared without bias and forming the bases for the insurance of lives for many millions of dollars.

Probably the reason for the failure to refer to medico-actuarial investigations is that physicians and surgeons do not sufficiently understand the object sought, the nature of the material available for study, and the method used in presenting the results of the analysis, each of which I shall now consider. With regard to the first mentioned, the companies desire to obtain information which will enable them to value the applicant's prospect of longevity; accordingly it is necessary to segregate the cases in which there apparently is organic disease and those with the so-called functional murmur. The companies can then determine what cases should be accepted at the regular rate of premium and which should be charged an extra premium on account of the additional hazard. This involves the valuation of applicants with heart defects according to the history and the physical signs. What is the meaning of a murmur? To what extent will statistics show that the longevity is modified by the presence of an abnormality? Is it scientifically possible to place the applicants in groups according to the deviations from standards accepted as normal and to insure them on a basis which is fair to them and to the company?

Cooperative Investigation.—With regard to the material available for study, life insurance companies have separate departments for mortality investigations and have records based on codes covering a large number of lives, such records being in the shape of perforated cards handled by modern machinery. They can follow the policyholder

*Vice president and chief actuary, New York Life Insurance Co.

until death, at which time the cause is obtained, or until he gives up his policy. For a generation the life insurance companies have been making cooperative studies, combining their material, and since 1909 there has been a committee of actuaries from the Actuarial Society of America and of physicians from the Association of Life Insurance Medical Directors in charge of these statistical researches. During that period many reports have been published, covering persons with all the principal types of impairment and those in hundreds of occupations involving hazard. For example, the volumes published in 1931 and 1932, entitled "Medical Impairment Study" (hereafter designated as M.I.S.), covered 2,100,000 policies in 125 groups or classes, involving, for instance, persons with heart murmurs, tuberculous family history, high blood pressure, rapid pulse, albuminuria, those with a history of renal colic, syphilis, gastric ulcers and all the gamut of human afflictions.

Method of Determining the Relative Mortality.—The method of presenting the statistics is very simple and does not require technical knowledge to understand. All that the readers need to know is that the mortality for the class under consideration is expressed in relation to the normal mortality, which is the death rate among "standard" risks.

At this point let me state that "standard risks" are those presenting no impairments or such minor ones that they are accepted at the regular premium rates, while "substandard" are those which present impairments of a more serious nature and hence are charged an extra premium or limited in some other way. If, for example, the relative mortality, taking account of the age of the insured and the duration of the insurance, was stated to be 150 per cent, it means 50 per cent higher than the normal or standard mortality; and this is the same as an extra death rate of 50 per cent. Thus, if the *extra* mortality among persons with a certain type of heart murmur was 50 per cent, then the companies had 50 per cent more deaths than among a corresponding group of lives considered to be "standard" or normal. Another way to look at the method of recording relative mortality is, that if the extra mortality were 50 per cent then there would be 150 deaths in the heart group against 100 in a similar group of the same ages and duration of insurance but without that impairment. In this article I shall always refer to the extra mortality in each class. The physician in reading this article need not concern himself with the various mortality tables used in determining the normal death rate. The general mortality of the insurance companies has improved but the ratios now presented take account of such changes. From the foregoing explanation it will be seen that the mortality among "standard lives" represents the "control" group against which all abnormal classes are measured.

In dealing with the mortality I refer to that from all causes among persons, who, when insured, showed some abnormality of the cardiovascular system. In several of the classes the death rate from heart disease will be given.

Nomenclature.—With the purpose of separating the applicants having organic heart disease from those without it, the insurance companies, in the years prior to 1925, coded heart murmurs under functional, mitral regurgitation, aortic regurgitation, and aortic obstruction. The clinical criteria for separating organic heart disease from nonorganic or functional are not well defined. For example, given a systolic murmur at the apex, does the fact that the murmur is transmitted lend weight to the probability that the murmur is caused by an organic defect? Or again is the same kind of a murmur associated with enlargement of the heart more significant than when this murmur is found in a heart of normal size? It was questions of this nature that led the companies in 1925 to adopt a new method of coding. In that year they began to regard the heart impairments according to the clinical description of the murmur found by the medical examiner. An outline is presented in which the old and new methods of classification are compared approximately:

Classification Prior to 1925	Classification of 1925 and Later
Functional Murmurs	Apex murmur, systolic, constant, not transmitted.
	Apex murmur, systolic, inconstant.
	Basic murmur, aortic area, systolic, constant, not transmitted.
	Basic murmur, aortic area, systolic, inconstant.
	Basic murmur, pulmonic area, systolic, constant, not transmitted.
Mitral Regurgitation	Apex murmur, systolic, constant, transmitted to the left.
Mitral Obstruction	Apex murmur, presystolic or diastolic, constant.
Aortic Obstruction	Basic murmur, aortic area, systolic, constant, transmitted upward.
Aortic Regurgitation	Basic murmur, aortic area, diastolic, constant, transmitted downward.

To aid in understanding the methods of the companies a special form of medical examination in connection with the heart appears in the appendix.*

*Special instructions for examination of the circulatory system are given in a booklet issued by the medical department for the guidance of our examiners in making examinations for the company. A copy of these instructions is included in the appendix.

RESULTS OF STUDIES

In order to give an idea of the importance to be attached to each group, the number of deaths will be shown. In Table I the two principal classes in this study (M.I.S.) of the so-called functional murmurs are given separately and the other two are combined—all cases being without hypertrophy.

TABLE I

TYPE OF MURMUR—NOT TRANSMITTED	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %
A. Constant systolic apex murmur	234	56
B. Constant systolic basic murmur, pulmonic area	124	12
C. Inconstant systolic apex murmur, also constant systolic basic murmur, aortic area	94	35

A fifth class closely related to these—inconstant systolic basic murmur in the aortic area was not studied in the M.I.S.

An interpretation of Table I may be of value at this point. The deaths among persons with a constant systolic apex murmur, not transmitted, were 234 but there would have been only 150 in a corresponding group without that impairment. Therefore the relative mortality was 156 per cent or an extra death rate of 56 per cent.

The material in Table I included only those lives which had been charged an extra premium on account of the impairment (substandard risks). If the data on risks accepted at the regular rate (standard) had been included along with the substandard, the mortality would probably have been lower, as they were assumed to be the best grade only.

The published experiences of life insurance companies have shown an increasing *relative* mortality with advancing age under those classified as "functional" murmurs. For organic murmurs the reverse has generally been noted. The cases classed as constant systolic apex, not transmitted, in Table I apparently contained an appreciable proportion of murmurs due to organic changes which has had its effect upon the percentages when arranged by age of the life insured. This is indicated in Table II, where classes B and C have been combined.

TABLE II

"FUNCTIONAL" HEART MURMURS—WITHOUT HYPERTROPHY. EXPERIENCE OF PRINCIPAL COMPANIES TO 1928

	A—CONSTANT SYSTOLIC APEX MURMUR		B AND C—OTHER MURMURS MORE TRULY "FUNCTIONAL"	
AGES AT DATE OF ISSUE	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %
15 to 34	103	84	85	1
35 to 44	68	61	65	16
45 and over	63	22	68	68
All	234	56	218	21

It seems probable that a marked proportion of the cases in group A were murmurs due to organic lesion, although no evidence, other than the murmur, was found by the medical examiner. In the group obtained by combining B and C the mortality is distinctly above the standard or normal except at the younger ages. This is in accordance with medical expectation where the murmurs at the younger ages are frequently associated with adolescence. Opinions differ, however, with regard to the middle and older ages. Is the extra mortality due to errors in diagnosis or do some of those classified as "functional" murmurs presage organic lesions?

The insurance companies recognize that all of the five murmurs are not of equal significance. Several companies, for example, treat applicants with an inconstant systolic apex murmur and those with a constant systolic basic murmur over the pulmonic area, slightly more liberally than those with the other three types of "functional" murmurs. Perhaps when more data have accumulated, a different alignment may be found.

An investigation made this year by the New York Life Insurance Company showed an extra mortality of 39 per cent (217 deaths) in the group of constant systolic apex murmurs not transmitted, accepted as impaired risks and an appropriate additional premium charged therefor. When the material was divided into policies issued from 1915 to 1924 and those from 1925 to 1934 the company had a more favorable experience in the latter than in the former, probably due to better diagnosis. A very carefully selected group with this heart defect might have a mortality only slightly above the normal.

In dealing with a large class there are many subdivisions, reflecting the variations from the average mortality. If, for example, the extra mortality in a class of heart murmurs was 50 per cent, a subdivision into several categories might indicate an extra 25 per cent in the one-tenth most favorable cases and 75 per cent among the one-tenth least favorable.

Judging from the experience of the life insurance companies a functional murmur should not be disregarded, certainly not after middle life. The companies have a method of rating each risk, whereby differentiations are made not only by type of murmur but also by age. For example, the extra mortality might be assumed to be 10 per cent at age 30 for a person with a constant systolic apex murmur not transmitted, but 35 per cent at age 45.

An analysis of the causes of death in the collective investigation (M.I.S.) shows that there were 94 deaths from organic disease of the heart among the cases accepted at substandard rates with functional murmurs, and there would have been 23 deaths in a corresponding group of lives without that impairment. In other words, the death rate from organic heart disease was four times the normal.

Organic Heart Murmurs.—In the preceding section we have considered the so-called functional murmurs and shall now turn to the organic ones. I am conscious of the differences of opinion among the specialists with regard to the importance of the systolic murmur. There have been wide ranges in thought from the early days when such a murmur was considered to indicate clearly some damage to the organ, to a recent period when it was stated by certain authorities to be of minor importance. I am not so much concerned, however, with these diverse opinions as with the actual mortality results of insuring persons with the various types of murmur. In determining the condition of the heart the companies must rely on examinations made by men of widely different backgrounds, ranging from physicians with ordinary training to the highest specialists in the profession. The statistical evidence, therefore, is based on the aggregate opinion of the medical profession, and, on the average, the companies get a reasonably correct statement of the clinical condition as they select their examiners carefully. The physician in the small town or in the country district may not have the specialized training of his metropolitan brother, but he is likely to have a valuable knowledge of the applicant's habits and manner of life.

Among applicants for life insurance the most common form of heart murmur is a constant systolic apex murmur, transmitted to the left. The data were divided according to degree of enlargement of the heart (hypertrophy) but no exact definition can be given of slight or moderate hypertrophy.*

The results of the cooperative investigation made by the principal companies is given in Table III.

TABLE III

MEDICAL IMPAIRMENT STUDY (1929)
CONSTANT SYSTOLIC APEX MURMUR, TRANSMITTED TO LEFT

	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %
Without hypertrophy	1,231	124
With slight hypertrophy	394	134
With moderate hypertrophy	196	376

The opinion held twenty-five or more years ago that moderate hypertrophy was of little moment if properly compensated is evidently incorrect. In fact the experience of the companies seems to show that the extent of the hypertrophy indicates the degree of the valvular damage. Nature is probably trying to compensate for the leakage by increasing the thickness of the heart muscle.

*It will be noticed from the heart chart that the medical examiner is expected to indicate the size of the heart both on the diagram and by measurements. He is also asked to state his opinion as to the degree of hypertrophy, if any. This opinion is given due weight at the home office in making the classification. In many cases further studies are made, including roentgenograms.

This phase of heart murmur is so vital that I am submitting an important contribution to the subject, based on recent statistics of the New York Life Insurance Company. The data are divided into two decennial periods according to the years in which the policies were issued. All cases were excluded where histories of rheumatism, chorea, tonsillitis, or similar infection were given.

TABLE IV

EXPERIENCE OF THE NEW YORK LIFE TO 1935
CONSTANT SYSTOLIC APEX MURMUR TRANSMITTED TO LEFT

WITHOUT HYPERTROPHY	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %
Policies issued 1915 to 1924	1,132	113
Policies issued 1925 to 1934	258	104
Total	1,390	111
WITH SLIGHT HYPERTROPHY		
Policies issued 1915 to 1924	222	133
Policies issued 1925 to 1934	116	227
Total	338	159
WITH MODERATE HYPERTROPHY		
Policies issued 1915 to 1924	144	227
Policies issued 1925 to 1934	53	366
Total	197	256

The evidence is convincing that a constant systolic apex murmur, transmitted to the left, is a serious impairment, with an anticipated mortality on the average of at least double the normal, if without enlargement. The *extra* mortality of the principal companies to 1928 in that class was 124 per cent and in the New York Life to 1935 it was 111 per cent, the amount of the data in both studies being too large to controvert the results. The death rate from heart diseases was far above the normal; 8, 10, and 15 times the normal in the three classes listed in Table IV. In fact, 65 per cent of the total number of deaths in the group with moderate hypertrophy was from heart affections.

With regard to slight hypertrophy, under the same kind of murmur, the extra mortality was 134 per cent in the cooperative investigation and 159 per cent in the recent research of the individual company—results which cannot be disregarded. With moderate hypertrophy the mortality is further apart but is evidence that an extra mortality of at least 250 per cent (three and one-half times the normal death rate) must be expected on the average.

Before leaving this type of heart murmur I should like to deal with a history of rheumatism associated with it. Fifty years ago such a condition was considered to be very serious and recent investigations have confirmed that early impression (Table V).

It is admitted that the companies do not get a history of infection in all cases where it has occurred, but the evidence is clear that an attack of rheumatism followed by this heart murmur is of major importance.

TABLE V

CONSTANT SYSTOLIC APEX MURMUR, TRANSMITTED TO LEFT, WITH A HISTORY OF RHEUMATISM OR CHOREA

MEDICAL IMPAIRMENT STUDY (1929)

	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %
Without hypertrophy	307	231
With slight or moderate hypertrophy	158	322

The findings in Table V have been confirmed by the more recent experience of the New York Life. Combining the different kinds of infection—rheumatism, chorea, tonsillitis, and scarlet fever—an extra mortality was experienced under the above type of murmur of 112 per cent (289 deaths) without hypertrophy, 196 per cent (145 deaths) with slight, and 341 per cent (154 deaths) with moderate hypertrophy. Based on these findings and similar studies the companies in the aggregate provided for an extra mortality by charging suitable extra premiums.

In the joint experience of the companies, the largest group with heart murmurs was divided into two groups, depending on the nature of their occupation—the white collar class, and those in heavy manual labor—excluding occupations for which an extra charge was made. Without entering into details it may be said that there was a distinctly higher death rate among the latter than among the former, other conditions being alike. If, for example, the extra mortality was 100 per cent among the white collar class, it would be approximately 150 per cent among the heavy manual workers.

I shall now deal briefly with three more of the serious forms of heart murmurs, as revealed by our life insurance companies' records (Table VI).

TABLE VI

MEDICAL IMPAIRMENT STUDY (1929)
WITHOUT HYPERTROPHY

TYPES OF MURMUR	NUMBER OF DEATHS	EXTRA MORTALITY OVER NORMAL, %
Constant systolic basic murmur, aortic area, transmitted upward	134	157
Constant diastolic basic murmur, aortic area, transmitted downward	34	357
Constant apex murmur, presystolic or diastolic.	41	380

The number of deaths in all but the first group is too small to give definite conclusions as to the exact mortality, but allowing a substantial margin for fluctuations the rates of extra mortality indicate the degree of hazard approximately.

Hypertrophy Without Murmur.—In only a small proportion of the applicants for insurance do we find hypertrophy without any kind of

a heart murmur; the companies generally provide for an extra mortality of about 50 per cent with slight, and of 75 per cent with moderate hypertrophy. This is partly based on a recent investigation which showed an extra mortality of 88 per cent (85 deaths) with slight or moderate hypertrophy.

History of Murmur.—What of the cases where there is a history of a murmur but none can be found now? The companies have not published anything of moment in this line but their practice reflects the point of view of their medical directors and actuaries. The day has passed when a murmur, apparently organic, heard by a reliable examiner in recent years is entirely disregarded in valuing the risk. Time and again a man dies of heart disease a year or two after the most careful examination, including electrocardiogram and roentgenogram, had failed to disclose any defect, yet there was a history of such a finding at an earlier examination. In this I refer not to difference of opinion with regard to the character of the murmur but to the presence of the murmur itself. I leave the answer to the heart specialists. Was the report of a murmur as organic a year ago by a reliable examiner which is not apparent now, an error of diagnosis or what was the fact?

Heart Murmur With a History of Other Impairments.—The question may probably be asked:—Have the companies any reliable information regarding mortality where there is a murmur with a *history* of rapid pulse, high blood pressure, albuminuria, or glycosuria, not now found? The answer is that the result of such a study was published in 1934 which proved that a history of these impairments added decidedly to the hazard. Although not found at the time of examination a weakness is indicated which makes the persons in this class less able to stand the effect of the heart murmur, and a return of the rapid pulse, albuminuria, and the other diseases is more likely than their occurrence among persons who have never had these defects.

Heart Murmur With Overweight.—At one time the opinion was freely expressed among physicians that overweight was a serious addition to a heart murmur. It may not be generally known that marked overweight in itself is a distinct impairment. For example, among persons who are 35 per cent overweight and insure at age 40 the companies provide for an extra mortality of 45 per cent and for those at age 50, of 55 per cent. No conclusive statistical evidence has yet been brought forward to show the mortality among those who combine marked overweight with a heart murmur. The companies are inclined to assume that the extra mortality is the sum of those arising from the respective impairments.

Factors in Connection With Murmurs.—I am not unmindful that there are many more factors to take into account than those already

mentioned—such as the habits of life, and the strength of the inhibitions. The clinician is primarily interested in the individual and the actuary in the group of lives, after the individuals are classified by the medical profession. In consulting with his patient the physician tries to bring out all factors favorable or unfavorable to recovery or to prolonging life. This means almost an infinite variety of types, which the actuary would find it necessary to consolidate into a comparatively few groups so as to get a sufficient number of persons in each to justify his conclusions.

To avoid misunderstanding it should be mentioned that the mortality ratios in this article do not necessarily represent the death rate among those who present themselves to heart specialists. On the one hand the specialist sees many in poor health who would not be accepted by the insurance companies and on the other there is a twofold selection involved in connection with applicants for insurance (a) by the company in determining what risks should be accepted and on what terms and (b) by the applicant who decides whether or not it is to his interest to accept the policy. The interplay of these two factors (a) and (b) may lead to results which are difficult to interpret. On the whole, however, it may be said that the mortality indicated in the insurance companies' investigations would approximately represent the additional death rate among those with the impairments in question, provided they were otherwise in good health and had no other major impairments.

Clinical Records.—The actuary has given the results of his researches to the world and is most desirous of comparing them with those of the heart specialist. The difficulties of the latter are great. He is not always a methodical man who keeps his records in first class shape for research. He is naturally more interested in keeping his clients in health than in collaborating with a statistician. The principal difficulty, however, lies in his inability to keep track of his patients, to determine whether they are living, and if not, the dates of death. He may see many of them only once on consultation, while those in clinics too frequently disappear from observation. It is hoped that these obstacles will be overcome in a measure in the case of clinical records, through cooperation with an actuary whose experience with mortality problems has been extensive. A comparison of studies based on the records of clinicians and on those of insurance companies may prove to be of great value.

Appendix

Instructions for Examination of the Circulatory System

It is suggested that, following examination of the heart when quiet, the applicant be requested to bend over, touching the floor six or eight times. This will bring out many murmurs that otherwise would be missed.

Transmission of Murmur.—Indicate by arrow on heart chart whether it is transmitted to axilla or back, or both, in the case of apical murmur; or to vessels of neck or across sternum to the opposite side in basic murmurs. If a poorly defined murmur is discovered, note findings with applicant in recumbent position; also with breath held with chest completely inflated and deflated. Observe effect of inspiration on murmur. Be on the lookout for any dyspnoea, cyanosis or marked and prolonged overaction of heart with failure to return to normal after three minutes' rest.

Cardiac Hypertrophy.—Determine if this condition exists by percussion with applicant erect in addition to noting point of maximum intensity of the apical beat. If the outer heart border reaches slightly beyond the nipple line, record moderate hypertrophy; if well within the nipple line, none. Record a little hypertrophy only after careful examination and when quite certain the outer border lies between these two points.

History of Acute Infectious Disease.—Give exact month and year of any acute rheumatic fever, tonsillitis or any other infection or acute illness which may have been an etiological factor.

Blood Pressure Observations.—In order to remove any psychic element the blood pressure should not be taken when the applicant is obviously nervous or apprehensive. It is advisable to distract the applicant's attention from the procedure by conversation. If the systolic pressure is found to be abnormally high, or the diastolic over 100, repeat the observation at the close of the examination. Be sure there is no faulty adjustment of the cuff of the apparatus and the arm is not hyperextended, which may partially destroy the apposition of the brachial artery to the cuff. Note any increase of the pulse pressure. A slight increase is frequently noted in mitral regurgitation and aortic obstruction, a decided increase in aortic regurgitation. With such a finding further auscultation of the heart sounds is indicated. Be sure to specify at which phase the diastolic pressure is recorded.

Character and Rate of Pulse.—Be sure that any pulse rate over 88 is not due to psychic disturbance and make a later observation. If pulse is persistently rapid, look for goiter or pulmonary signs or elevated temperature. Count the number of irregularities or intermissions over a whole minute. If pulse is irregular or intermittent, exercise applicant and report if abnormality increases or disappears. Note if the pulse be high tension, dicrotic or Corrigan types or weak and thready in character. Make the diagnosis of myocarditis with great caution and only in the presence of the usually accepted signs—extreme irregularity or intermittency, pulsus alternans, weak and distant heart sounds, low blood pressure, etc.

HEMODYNAMIC STUDIES IN EXPERIMENTAL CORONARY OCCLUSION*

III. Denervated Heart Experiments

Milton Mendlowitz, M.D.† Gerhard Schauer, M.D., and Louis Gross, M.D.
New York, N. Y.

IN TWO preceding reports,[1, 2] we demonstrated that ligation of the left anterior descending coronary branch in dogs was followed by an immediate decrease in cardiac output without any corresponding diminution in circulating blood volume. The absence of this diminution in blood volume ruled out the possibility that there was any direct loss of blood or plasma in or about the injured myocardium of sufficient magnitude to account for the decrease in cardiac output.[3, 4] It also precluded the possibility that a toxic substance, such as histamine, was liberated from the injured myocardium in sufficient quantities to trap the circulating blood in the peripheral capillary bed and thus diminish minute volume.[5] The possibility remained, however, that nervous reflexes from the heart to the peripheral blood vessels and to the heart might affect the cardiac output.

In these studies, therefore, we employed a procedure with the object of interrupting all the motor and sensory impulses to and from the heart respectively. This involved resection of both thoracic sympathetic chains from stellate through sixth or seventh thoracic ganglia, as well as bilateral sympatheticovagotomy in the neck. The aortic depressor nerves were severed with the vagosympathetics, whereas the nerves from the carotid sinuses were left intact. Although White[6] considers them to be of no importance even if they exist, possible sensory pathways via the cardiac nerves and cervical sympathetic ganglia and thence directly into the cervical spinal cord would, according to Braeucker[7] and Heinbecker,[8] still be left intact by these procedures. With these reservations in mind, then, we were dealing with a denervated heart.

The prevalent immediate cause of death after the final as well as the preliminary procedures was pneumonia. Seventy-five per cent of the total number of animals initially subjected to operation died before the final experiments could be performed. In the remaining 25 per cent, two groups with ten dogs in each, the following procedures were successfully carried out. Under nembutal anesthesia, the right chest was opened in the fourth interspace. The right lung was compressed anteriorly and mesially with packs which were held in place

*From the Laboratories of The Mount Sinai Hospital, New York, N. Y.
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†George Blumenthal, Jr., Fellow.
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by lung retractors. The sympathetic chain, thus exposed, was resected from the sixth or seventh thoracic ganglion up to and including the stellate. The packs were then removed and the chest closed in the usual way. One week later the left chest was opened in the fourth interspace under anesthesia. The sympathetic chain was exposed as before, and resected from the sixth or seventh thoracic ganglion up to and including the stellate. The packs were then removed and in one group of ten dogs, the double carrick bend was placed around the left anterior descending coronary branch in the manner described in the preceding report.[2] In the other group of ten dogs (controls), the knot was placed around relatively avascular left ventricular muscle. The chest was then closed in the usual manner. One week later the animals were again anesthetized. Both vagosympathetic trunks in the neck were severed, following which the physiological studies were carried out in series as described in our first report.[1] The left anterior descending coronary branch or some left ventricular muscle, in the two groups, respectively, was then ligated from the exterior of the chest and the studies repeated. Electrocardiograms were taken before and after the various steps in the procedure. None of the animals survived the bilateral sympatheticovagotomy for more than twenty-four hours. Complete autopsies were done on all the animals which succumbed.

PRELIMINARY OBSERVATIONS

Following the right sympathectomy, there was an appreciable retardation in pulse rate. The electrocardiographic changes* were similar to those found with an increase in right vagal tone.[9] This apparent increase in vagal tone was probably only relative to the decrease in opposing sympathetic tone.[10] At the end of a week these changes became less marked.

After left sympathectomy, there was usually a further slowing of the heart rate although this was not invariable. The electrocardiographic changes were now similar to those with an increase in left vagal tone.[9] In several cases heart-block developed and was usually fatal. In the others, the manifestations of relatively increased vagal tone tended to subside during the course of a week.

After bilateral sympatheticovagotomy in the neck, several changes took place. The respirations became slower and irregular in depth. This made the determination of the ether circulation time more difficult and therefore less reliable. There was no irregularity, however, in the rate of oxygen consumption and hence no difficulty from this source in the estimation of the cardiac output. The temperature tended to fall somewhat more than in previous experiments.[1, 2] The cause for this greater fall was obscure. It might have been due in

*To be reported in detail in a separate communication.

part to denervation of the lungs, which in the dog are very important in the regulation of temperature.[11] The arterial blood pressure was now subject to only minimal fluctuations in contrast to its lability in our previous experiments. There was occasionally a slight increase in heart rate after both vagosympathetic trunks were severed. Except for this occasional change in rate, the electrocardiogram was now relatively normal. The intravenous injection of sodium cyanide had a paradoxical effect.[12] Whereas the injection was followed in previous experiments by a retardation in heart rate and electrocardiographic evidence of increased vagal tone, in these animals with denervated hearts there was an acceleration.

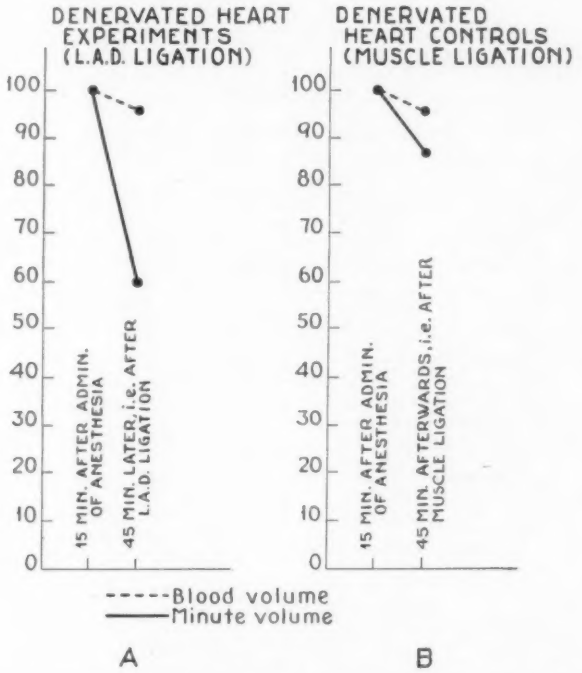

Fig. 1.—Average per cent changes in cardiac output and in blood volume per square meter of surface area.

RESULTS IN FINAL EXPERIMENTS

The effect of ligation of ventricular muscle on the cardiac output (Table I) was not appreciably different from that observed in all the control studies done in previous experiments.[1, 2] There was a moderate immediate decrease in average minute volume (Fig. 1*B*).

The effect of ligation of the left anterior descending coronary branch in these animals (Table II) was not significantly different from the effect of ligation in previous experiments.[1, 2] The immediate decrease in average cardiac output was definitely more profound than in the control group (Fig. 1*A*). In the graph demonstrating the individual case

TABLE I

DENERVATED HEART CONTROL EXPERIMENTS

DOG NO. AND SEX	DATES OF OPERATIVE PROCEDURES: RIGHT SYMPATHECTOMY (T1-6)	DATES OF OPERATIVE PROCEDURES: LEFT SYMPATHECTOMY (T1-6) LIGATURE PLACED AROUND MYO. FIBERS	DATES OF OPERATIVE PROCEDURES: BILATERAL VAGOTOMY AND LIGATION	TIME OF TESTING	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT MINUTE VOLUME PER SQ. METER IN C.C.	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS—GRAMS PER CENT	BLOOD PRESSURE: ARTERIAL IN M.M. OF MERCURY	BLOOD PRESSURE: VENOUS IN CM. OF WATER	CIRCULATION TIME: ETHER IN SEC.	CIRCULATION TIME: CYANIDE IN SEC.	REMARKS
74F ♂	9/21/36	10/ 1	10/ 8	Preligation*	14.4	101.4	130	118.0	5.23	3394	2086	57	6.36	148	0	5.0	8.5	10/9 Dog died. Autopsy: Left chest wound gangrenous; atelectatic pneumonia of both lungs; thread torn through muscle; L.A.D. patent; no infarct.
				Postligation	14.4	100.0	136	112.0	6.55	2572	1948	58	6.06	150	0	5.5	9.0	
76F ♂	9/21	10/ 1	10/10	Preligation	7.0	97.0	102	66.0	3.81	4223	2073	51	5.49	118	0	4.5	12.5	10/11 Dog died. Autopsy: Atelectasis of both lungs; muscle ligated; L.A.D. patent; no infarct.
				Postligation	7.0	96.0	100	63.0	4.08	3765	1935	58	5.77	110	0	4.0	13.5	
30G ♂	10/22	10/29	11/ 5	Preligation	13.0	100.6	116	115.0	3.22	5765	2583	55	5.55	113	3.5	6.5	17 ?	11/6 Dog died. Autopsy: Lungs congested; muscle ligated; L.A.D. patent; no infarct.
				Postligation	13.0	100.3	111	115.0	3.80	4880	2364	63	5.23	105	2.5	6.5	13.5	

*Ligation of left ventricular muscle.

TABLE I—CONT'D

46G ♂	10/30	11/ 6	11/12	Preligation	6.6	97.5	148	69.5	2.67	6605	2158	53	6.34	135	1.0	3.5	8.0	11/13 Dog died. Autopsy: Bilateral bronchopneumonia; muscle torn through by thread; L.A.D. patent; no infarct.
				Postligation	6.6	94.7	134	73.0	3.13	5920	2064	57	6.39	110	0	4.0	9.0	
84G ♂	11/14	11/21	11/28	Preligation	17.5	99.6	110	112.0	3.89	3810	2220	67	5.53	143	2.5	7.5	14.0	11/28 Dog killed. Autopsy: Muscle ligated; L.A.D. patent; no infarct.
				Postligation	17.5	97.0	110	108.0	5.68	2514	2098	67	6.02	148	2.3	6.5	12.0	
94G ♂	11/16	11/27	12/ 3	Preligation	15.8	97.0	108	163.0	3.32	6950	2286	53	6.47	130	0	8.5	15.0	12/3 Dog killed. Autopsy: Muscle ligated; L.A.D. patent; no infarct.
				Postligation	15.8	95.8	104	148.0	4.43	4736	2183	53	6.49	140	0	10.0	14.0	
99G ♂	11/17	11/27	12/ 4	Preligation	23.0	102.3	124	183.0	3.85	5240	3298	62	6.15	145	4.5	4.5	13.0	12/4 Dog killed. Autopsy: Muscle ligated; L.A.D. patent; no infarct.
				Postligation	23.0	101.2	124	173.0	3.93	4860	3258	65	6.28	145	5.5	4.5	11.0	
3H ♀	11/18	11/30	12/ 7	Preligation	10.8	98.0	120	108.0	3.31	5938	2755	63	5.82	133	1.5	7.5	12.0	12/8 Dog died. Autopsy: Bilateral hemorrhagic pleural effusion; lungs atelectatic; scattered pneumonic patches; muscle ligated; L.A.D. patent; no infarct.
				Postligation	10.8	95.0	112	99.0	2.26	7960	2496	67	5.72	130	2.0	6.0	10.0	
23H ♀	11/25	12/ 2	12/10	Preligation	8.8	99.6	154	91.0	2.98	6383	2320	70	4.19	118	0	6.5	14.0	12/10 Dog died. Autopsy: Muscle ligated; L.A.D. patent; no infarct.
				Postligation	8.8	97.4	130	87.0	4.43	4100	2508	73	4.17	105	3.4	?	indef.	
12H ♂	11/24	12/ 1	12/ 8	Preligation	15.8	100.0	128	116.5	3.96	4165	2660	71	5.51	105	1.5	5.5	15.0	12/8 Dog killed. Autopsy: Muscle ligated; L.A.D. patent; no infarct.
				Postligation	15.8	100.0	114	105.0	3.41	4360	2535	71	5.64	105	1.5	6.0	13.0	

TABLE II

DENERVATED HEART EXPERIMENTS

DOG NO. AND SEX	DATES OF OPERATIVE PROCEDURES: RIGHT SYMPATHECTOMY (T1-6)	DATES OF OPERATIVE PROCEDURES: LEFT SYMPATHECTOMY (T1-6) LIGATURE PLACED AROUND L.A.D.	DATES OF OPERATIVE PROCEDURES: BILATERAL VAGOTOMY AND LIGATION	TIME OF TESTING	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT MINUTE VOLUME PER SQ. METER IN C.C.	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS—GRAMS PER CENT	BLOOD PRESSURE: ARTERIAL IN MM. OF MERCURY	BLOOD PRESSURE: VENOUS IN CM. OF WATER	CIRCULATION TIME: ETHER IN SEC.	CIRCULATION TIME: CYANIDE IN SEC.	REMARKS
18F ♀	8/18/36	8/29	9/ 4	Preligation*	12.0	99.0	120	113.0	3.46	5558	2520	85	3.67	140	1.5	4.0	9.0	9/5 Dog died. Autopsy: Patchy bilateral bronchopneumonia; L.A.D. not patent; incipient infarct of indefinite extent.
				Postligation	12.0	98.6	120	75.0	4.18	3050	2280	85	4.14	130	1.0	5.0	9.0	
30F ♂	8/21	8/31	9/16	Preligation	12.5	100.2	122	88.0	3.25	4500	1952	76	5.06	120	1.0	5.0	13.0	9/17 Dog died. Autopsy: Lungs congested; L.A.D. not patent; infarct present.
				Postligation	12.5	98.0	108	93.0	5.07	3044	1880	77	4.49	108	1.5	5.0	15.0	
40F ♂	8/25	9/ 4	9/17	Preligation	9.6	101.4	136	88.0	3.73	4640	1989	58	4.03	125	1.5	5.5	13.0	9/18 Dog died. Autopsy: Old pericardial adhesions; L.A.D. not patent; incipient infarct of indefinite extent.
				Postligation	9.6	100.8	130	90.0	5.28	3357	1995	62	3.87	95	2.0	8.0?	17.5	

*Ligation of left anterior descending coronary branch.

TABLE II—CONT'D

64F ♂	9/18	9/26	10/ 5	Preligation	16.6	101.8	150	163.0	1.96?	11370?	2940	63	4.71	125	2.0	5.5	10.5	10/5 Dog died of ventricular fibrillation. Autopsy: L.A.D. not patent; no apparent infarct.
				Postligation	16.6	-	134	138.5	5.03	3770	2620	69	4.95	90	2.0	--	---	
68F ♂	9/19	9/29	10/ 6	Preligation	9.0	99.1	114	92.0	2.51	7550	2284	60	6.59	150	2.5	7.5	11.0	10/7 Dog died. Autopsy: L.A.D. not patent; incipient infarct.
				Postligation	9.0	98.3	114	131.0	7.03	3846	2134	67	6.51	140	2.5	5.0	13.0	
71F ♀	9/19	9/30	10/ 7	Preligation	12.7	99.0	106	119.0	3.88	5040	2576	50	6.23	112	2.0	4.0	9.0	10/8 Dog died. Autopsy: Lungs congested; L.A.D. not patent; incipient infarct of indefinite extent.
				Postligation	12.7	98.0	108	110.0	5.40	3340	2455	54	6.01	90	4.0	5.0	15.0	
4G ♀	10/10	10/20	10/26	Preligation	10.6	99.8	122	100.0	2.20	8390	1897	69	5.70	115	0.5	11.0?	10.0?	10/27 Dog died. Autopsy: L.A.D. not patent; infarct present.
				Postligation	10.6	96.6	118	79.0	3.92	3710	1835	70	5.96	115	2.0	5.5	21.5?	
18G ♀	10/17	10/28	11/ 4	Preligation	16.0	101.6	138	140.0	3.53	5570	4200?	93	5.64	122	1.0	3.5	11.0?	11/5 Dog died. Autopsy: Pneumonic patches in both lungs; L.A.D. not patent; infarct present.
				Postligation	16.0	101.8	132	135.5	5.37	3548	3836?	93	5.55	122	0	4.5	11.5	
22G ♀	10/17	11/ 2	11/10	Preligation	13.0	99.8	150	111.5	5.80	3110	2274	71	5.87	160	5.5	8.5?	11.0	11/11 Dog died. Autopsy: L.A.D. not patent; incipient infarct of indefinite extent.
				Postligation	13.0	99.6	158	97.0	6.38	2452	2446	71	5.70	120	0	5.5	9.5	
62G ♂	11/ 9	11/16	11/20	Preligation	17.0	101.2	136	168.0	7.39	3058	2662	98	5.28	145	0.5	--	13.0	11/21 Dog died. Autopsy: Lungs congested and atelectatic; L.A.D. not patent; infarct present.
				Postligation	17.0	101.0	128	129.0	8.51	2040	2645	88	5.37	145	2.5	4.0	16.0	

distribution with reference to immediate change in cardiac output (Fig. 2), there is evidence that the diminution in minute volume was consistent.

In contrast to previous experiments[1, 2] there was usually an immediate decrease in the arterial blood pressure following ligation of the vessel as against minimal changes in the control group. The ether and cyanide circulation times in both groups tended to be somewhat more prolonged than those reported previously. Contrary to our former experience, the average fall in temperature was greater in the control group than in the vessel ligation group. In view of the variable factor introduced by sympatheticovagotomy, it is impossible to evaluate

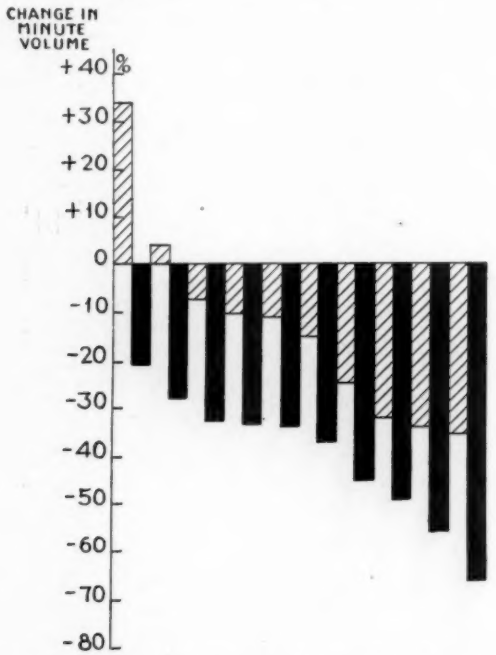

Fig. 2.—Individual case distribution with reference to the changes in cardiac output directly after the procedure.

this finding. Ligation of the artery was followed by the same characteristic electrocardiographic alterations previously observed,[13] namely, an elevation of the R-T transition in Lead I with or without an S-T depression in Lead III. Ventricular fibrillation was occasionally observed. These changes were never seen in any of the control experiments.

In other respects there were no essential differences between the findings in these experiments and those in the experiments in which the heart had not been denervated.[1, 2] The cyanide circulation time tended to be prolonged after ligation of the vessel, whereas the ether circulation time remained relatively unchanged. The blood volume

was usually slightly diminished in both the ligation and the control groups, and the erythrocyte count and the hemoglobin percentage together with the cell volume were usually slightly increased in both groups. The venous pressure was variable, and there were no significant changes in pulse rate or in serum proteins.

DISCUSSION

In these experiments all or most of the motor and sensory pathways to and from the heart respectively were interrupted. There was, nevertheless, a definite decrease in cardiac output without any corresponding change in blood volume following left anterior descending coronary branch ligation. The reduction in output could not, therefore, have been caused by reflexes from the injured myocardium to visceral or peripheral blood vessels or to the heart.

The immediate fall in blood pressure following vessel ligation in these experiments might in part be attributed to the absence of the masking effect of the usually wide fluctuations in vasomotor tone hitherto observed.[1, 2] Another probable factor was the interruption of some of the nervous pathways for compensatory vasoconstriction. That some vasoconstriction took place, however, is attested to by the fact that in most instances the decrease in cardiac output was proportionately greater than the fall in blood pressure.

It may be argued that occlusion of the left anterior descending coronary branch primarily caused only a slight cardiogenic diminution in minute volume, that this initiated a compensatory reflex vasoconstriction via the carotid sinus,[14, 15] and that this vasoconstriction was responsible for a great part of the observed decrease in cardiac output by impeding the venous return to the heart. Inasmuch as the carotid sinus and other possible vasomotor mechanisms[14] were left intact in our experiments, it is impossible to refute this argument conclusively. There are, however, considerations which weaken the force of such a contention. It is known, for example, that neither experimental[17] nor clinical[18] hypertension, presumably associated with a generalized vasoconstriction, diminishes the cardiac output. It is therefore likely that such vasoconstriction as probably occurred in our experiments did not diminish the venous return to the heart and hence played no predominant part in the significant decrease in cardiac output observed.

It is evident, therefore, that the diminution in cardiac output following left anterior descending coronary branch occlusion in the dog is largely, if not entirely, primarily cardiogenic. In other words, it is attributable to the inability of the left ventricle to expel all the blood it receives. As a result of this, there is an accumulation of blood in the pulmonary veins and capillaries. We are dealing, then, in these experiments with (1) cardiogenic hypokinetic circulatory failure and (2) left ventricular congestive failure.

SUMMARY

1. A technic is described for ligation of the left anterior descending coronary branch in the dog after denervation of the heart.

2. The changes following ligation of the vessel consist of a fall in cardiac output and blood pressure and a prolongation of the cyanide circulation time.

3. The hypothesis that the decrease in minute volume is neurogenic is considered, with some reservations, unsubstantiated.

4. The preponderance of evidence supports the theory that the decrease in cardiac output is cardiogenic.

5. The ligation of the left anterior descending coronary branch in the dog is followed by cardiogenic hypokinetic circulatory failure and left ventricular congestive failure.

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THE ELECTROCARDIOGRAPHIC CHANGES IN ACUTE PERICARDITIS

A Clinical and Pathological Study*

Joseph B. Vander Veer, M.D., and Robert F. Norris, M.D.
Philadelphia, Pa.

THE diagnosis of acute pericarditis, especially of the purulent type, is often difficult. The frequency with which this condition is found post mortem, when clinically unsuspected, is well known. For several years, it has been recognized that patients with acute pericarditis, with and without effusion, and with hemopericardium, may show electrocardiographic changes of the RS-T segments and T-waves. The cause of these abnormalities has not been finally determined. The literature contains few reports of patients with acute pericarditis in which serial electrocardiograms were taken and in which complete pathological studies were done.

Schwab and Herrmann[1] reviewed the literature and reported seven cases of acute pericarditis. Although minor changes occurred in the electrocardiograms of all, only two cases showed significant elevations of the RS-T segments. In one of these, acute purulent pericarditis was present at autopsy, but a microscopic description of the myocardium was not given. No other post-mortem examinations were available. They felt that the positive deviations in the RS-T segments were caused by myocardial ischemia produced by the rise of intrapericardial pressure resulting from effusion. In one of the cases, however, a rapid tamponade from hemopericardium produced no alteration of the RS-T segments.

Scott, Feil, and Katz[2] differentiated the electrocardiographic changes of pericardial effusion from those of myocardial infarction and suggested that the electrocardiogram might be of diagnostic value in pericardial effusion. In a case of hemopericardium and in one of acute purulent pericarditis, elevated R-T segments returned to normal without drainage of the pericardial sac.

In a well-studied case of pneumococcic pericarditis, in which paracentesis and pericardiotomy were done, Harvey and Scott[3] reported elevation of the R-T segments in all leads, with return to normal before death. This return to normal was attributed to drainage of the pericardium. At autopsy "no coronary disease or gross myocardial damage was found."

In a patient with purulent pericarditis reported by Purks,[4] an electrocardiogram the day before death showed elevated R-T segments in

*From the Morris W. Stroud, Jr., Fellowship in Cardiology, the Medical Services, and the Ayer Clinical Laboratory of the Pennsylvania Hospital.

Leads I and II. At post-mortem examination a large pericardial effusion was associated with acute pericarditis and subjacent myocarditis.

Master, Romanoff, and Jaffe[5] studied 52 cases of pneumonia with daily electrocardiograms. In one case a marked elevation of the R-T segments was present in all leads on the day of death. This was the only case which showed pericarditis at autopsy. Foci of degeneration were found in the muscle fibers but no mention was made of the microscopic appearance of the pericardium or subjacent myocardium.

Koucky and Milles[6] recently reviewed the literature on stab wounds of the heart in which surgical repair was successful and serial electrocardiograms were obtained. They reported an additional case of stab wound of the anterior surface of the right ventricle in which recovery followed suture of the ventricle. Purulent pericarditis was proved on the fourth postoperative day and open drainage was instituted. Electrocardiograms on the first, fifth, and ninth days after operation revealed elevated R-T segments of about equal height in Leads I and II. In Lead III the R-T segment was normal or only slightly elevated.

In a patient with a stab wound involving the anterior descending branch of the left coronary artery, Elkin and Phillips[7] obtained electrocardiograms before, during, and after operation. A pericardial friction rub was present from the third to the sixth days. A teleroentgenogram on the fourth day showed evidence of pericardial effusion. The record taken before operation, during a period of extreme cardiac tamponade, was practically normal. Ten minutes after operation, slight elevation of the R-T segments was present in Lead I and slight depression in Lead III. Thirty-six hours after operation, the R-T segments were elevated in all leads but especially in Lead II. These changes persisted for several days with gradual return to normal.

In two cases of stab wounds of the heart involving the anterior surface of the left and right ventricles, respectively, Porter and Bigger[8] obtained frequent electrocardiograms. The tracing obtained fourteen hours after operation in Case 1 resembled that seen after anterior myocardial infarction. The records on the fourth and fifth days, however, showed elevated R-T segments in all leads, particularly in Lead II. In the second case, elevation of the R-T segments was present in all leads and again, after the second day, was most marked in Lead II. Pericarditis was not suspected clinically in either of these cases.

Barnes[9] analyzed the findings in seven patients with acute coronary occlusion in which the electrocardiograms were characterized by elevation of the R-T segments in the three limb leads. Because the usual reciprocal deviation of the RS-T segments in Leads I and III was lacking, localization of the infarct was difficult. From clinical and post-mortem studies, he concluded that electrocardiograms of this type after coronary occlusion were the result of a coincident pericarditis.

In a subsequent article, however, Wolferth and Wood[10] reported 10 cases with similar electrocardiograms. They ascribed this type of record to infarction involving both the anterior and posterior surfaces of the left ventricle. Post-mortem studies in two cases showed this lesion in both. No mention was made of the presence or absence of pericarditis. These authors logically explained this type of electrocardiogram as the summation effect of both anterior and posterior infarction.

Experimental studies in this field have been largely concerned with the production of electrocardiographic changes by increasing the intrapericardial pressure. Katz, Feil, and Scott[11] injected saline and oil into the pericardial sac of dogs. In some instances, the R-T segments were elevated in all leads. On release of pressure, the electrocardiograms returned to normal. These changes were thought to be the result of myocardial anoxemia. Herrmann and Schwab,[12] by increasing the intrapericardial pressure of goats, reduced the pulse pressure to minimal levels. In some animals, the R-T segments were elevated in four leads of the electrocardiogram. Diminished circulation to the posterior as well as to the anterior surface of the heart was advanced as the cause of the changes. As controls in studies of coronary ligation on dogs, Barnes and Mann[13] opened the pericardium and manipulated the heart without ligation of vessels. On the fourth and fifth days thereafter, elevation of the R-T segments occurred in two of three animals. Fowler, Rathe, and Smith[14] noted similar electrocardiographic changes in dogs when the pericardium was merely opened. Microscopically, inflammation of the epicardium extended into the adjacent myocardium. Degenerative changes were evident in the superficial muscle fibers. Pericardial adhesions were numerous. The authors attributed the electrocardiographic changes to myocardial damage.

In an effort to determine the cause of the electrocardiographic changes found in acute diseases of the pericardium, we have studied a variety of conditions in which acute pericarditis may occur. Serial electrocardiograms were taken in 63 patients with pneumonia or empyema. In this group there were 23 deaths and 18 autopsies. Five of these patients had acute pericarditis. Three cases of pericarditis secondary to uremia with two post-mortem examinations were likewise studied. In three patients with rheumatic pericarditis, no autopsies were obtained. Autopsies were obtained in three more cases of acute pericarditis. One of these was probably gonococcic; another followed a stab wound of the right auricle; and the last was a hemopericardium from a ruptured aorta. Six of the entire group had definite and similar changes in the electrocardiograms, and all were proved post mortem to have pericarditis. Two cases of uremia and two of pneumonia, with pericarditis at autopsy, had no such electrocardiographic changes. In all of the post-mortem studies numerous sections from

both auricles and ventricles were examined microscopically. We are reporting clinical and pathological studies on the six cases with "positive" electrocardiograms.

CASE 1.—(No. 38958.) B. E., a colored housewife, thirty-five years of age, was admitted to Medical Service A on Aug. 18, 1935. She complained of pains in the joints. The family and past medical histories were not significant except for an ectopic pregnancy in 1929. The patient dated her illness to February, 1935, when she noted pains in the knees, ankles, and wrists. She was up and about for three months, with little improvement. Persistent fever was noted after May. On August 5, the swelling of the joints became worse and the fever higher. During the illness, she lost 25 pounds in weight.

Examination revealed an emaciated, feverish, and "toxic" woman. Motion of both ankles and the right shoulder, wrist, and knee was extremely painful. The lungs were clear. A systolic murmur was heard at the apex of the heart. The rhythm was regular and the rate 120. A purulent urethral discharge was present and marked tenderness existed in the right adnexal region. Right femoral phlebitis was also noted. With rest in bed, the arthritic symptoms became less severe, but the temperature remained elevated. On October 29, however, the fever was high and peritonitis spreading from the pelvis was thought to be present. The arthritis was reactivated. X-ray studies of several joints showed destructive changes suggestive of gonorrheal arthritis. In December, marked bilateral cervical lymphadenopathy occurred which subsided after x-ray treatments.

Following a gynecological examination on Jan. 23, 1936, the temperature rose sharply, generalized abdominal pains were present, and the arthritis was aggravated. Continuing for several days, a pericardial friction rub was first heard on January 24. Because of a marked pulsus paradoxus on February 2, the pericardial sac was tapped through the fifth intercostal space in the anterior axillary line and 280 c.c. of yellow pus were aspirated. The specific gravity of this fluid was 1.020 and there were 19,350 cells, mostly polymorphonuclear neutrophiles, per cubic millimeter. Two days later, 450 c.c. of purulent exudate were again removed. No bacteria were demonstrated in either specimen on smear and culture. Inoculation of guinea pigs was negative for tuberculosis. The cardiac signs disappeared. The fever continued to be septic in type. Large bedsores occurred, and the patient died on March 13, 1936.

Of a large amount of laboratory data, the significant findings were two strongly positive gonococcus complement fixation tests, secondary anemia, normal leucocyte counts, with a shift to the left in the polymorphonuclear neutrophiles, and repeatedly negative blood cultures. Blood Wassermann and Kahn tests were negative. For electrocardiograms, see Fig. 1.

Autopsy (No. 5507).—The autopsy was done seven hours after death. Anatomical Diagnosis: Primary cause of death undetermined. History of former pelvic operation. Scar in lower abdomen. Absence of right fallopian tube and ovary. Fibrous adhesions between abdominal scar and stump of right broad ligament. Scarring of left fallopian tube. History of polyarthritis. Chronic adhesive pericarditis. Lobular pneumonia. Fibrous pleural adhesions of lower lobes of both lungs. Fibrous adhesions between capsule of liver and peritoneal surface of diaphragm. Fatty changes of liver. Focal necroses of liver. Acute splenic tumor. Calcification of renal tubules. Hyperplasia of bone marrow. Decubitus ulcers of right hip and lower back. Small scars of right side of neck. Calcified and caseous lymph nodes.

Pericardium and Heart.—Dense fibrous adhesions were present between the outer surface of the pericardium and the adjacent pleurae. Except in a few small areas over the ventricles, the pericardium and epicardium were firmly united by dense

fibrous adhesions. The heart and pericardium weighed 280 gm. The myocardium was pale, but showed no focal lesions. The endocardium, valves, and coronary arteries were not remarkable.

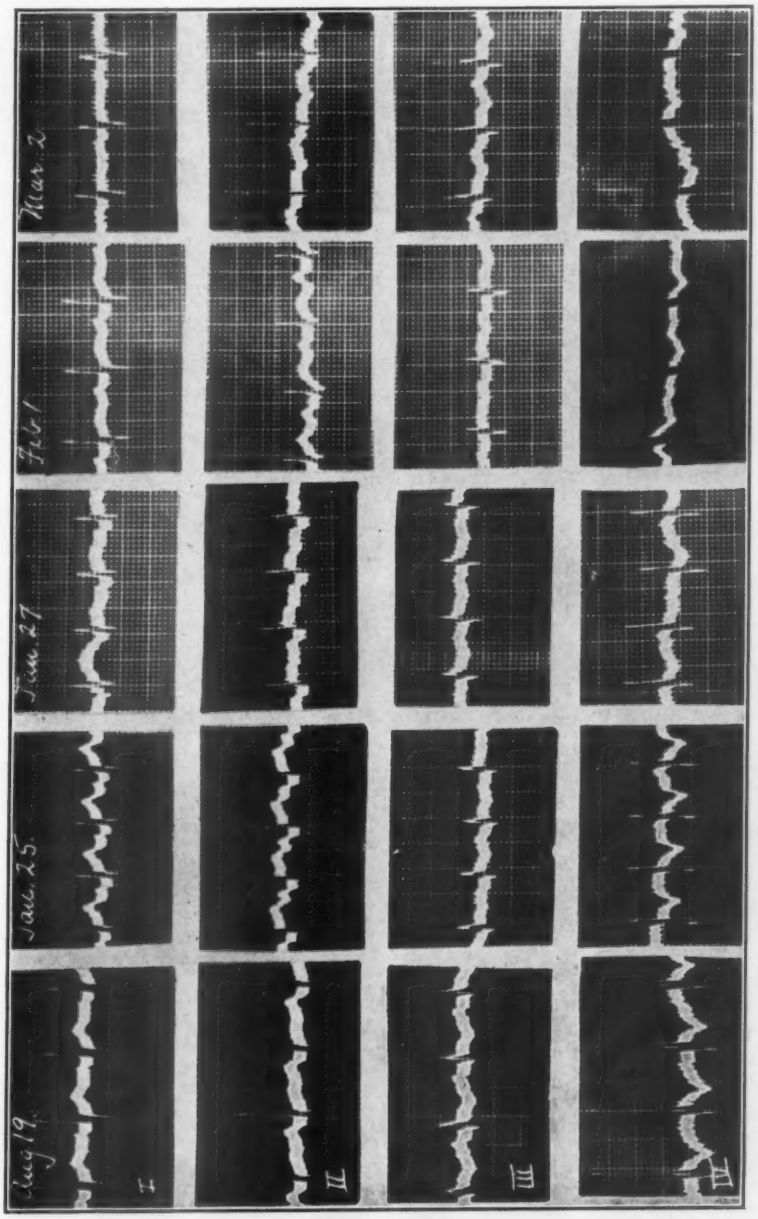

Fig. 1.*—Case 1. Acute gonorrheal (?) pericarditis. The first record was taken the day after hospital admission for acute arthritis. On January 24 precordial pain and a pericardial friction rub were noted. In the record of January 25 note the elevation of the R-T segment in Leads I, II, and III, greatest in Lead II. There is a gradual return toward normal as pericardial exudate accumulated (Feb. 1). On February 2 and 4 the pericardial sac was aspirated and considerable pus obtained. Some residual T-wave changes are seen in Leads I and II of the last record. A relatively deep Q-wave is seen in Lead III in some of the records. There is no essential change in the chest lead (Lead IV), taken with the precordial electrode at the apex area and the indifferent electrode on the left leg.

*Photographs by Mr. Emil Forney.

Microscopically, much of the fatty tissue of the pericardium and epicardium was replaced by scars, and the adhesions were also composed of hyaline fibrous tissue. Rarely were young capillaries and fibroblasts seen. Where adhesions were lacking, a little fibrin and a few round cells were present on the surface of the epicardium. In most areas scar tissue was in contact with the surface of the myocardium. Small

numbers of lymphocytes and plasma cells were present in the deeper layers of the epicardium, but none were seen among the muscle fibers and there was no interstitial scarring of the myocardium (Fig. 2). In many localities of both auricles and ventricles, however, the surface of the myocardium was exceptionally irregular as if groups of fibers had disappeared. No evidence of rheumatic inflammation or other abnormalities was seen in the heart.

Bacterial Studies.—No bacteria were demonstrated in the sections of lungs and no acid-fast bacilli or other organisms were seen in the liver or caseous mesenteric lymph nodes.

CASE 2.—(No. 40853.) L. D., a white man, forty-one years old, was admitted to Medical Service B on March 14, 1936. He complained of cough and generalized pain in the abdomen. He had had previous attacks of pneumonia in 1922 and

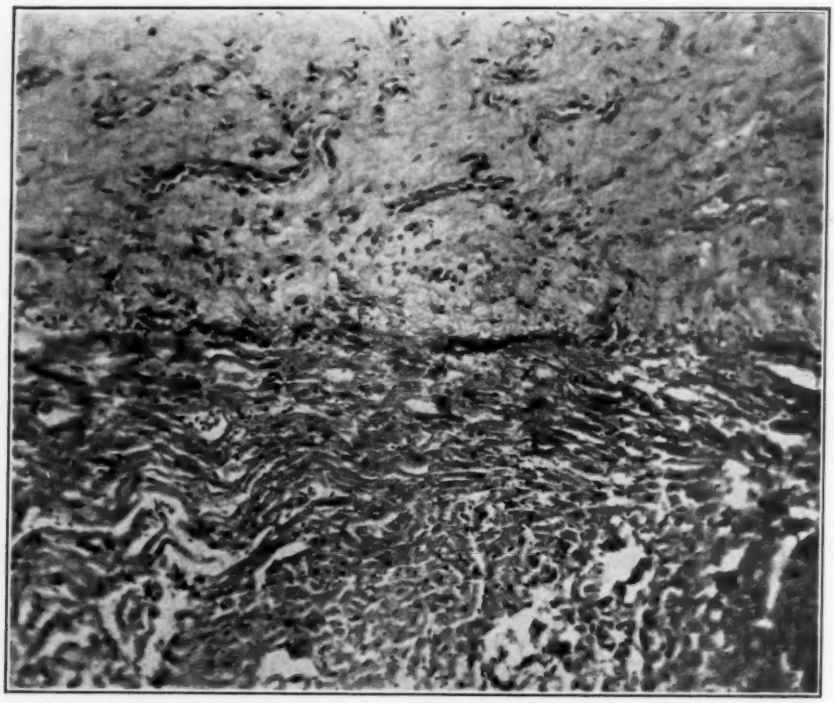

Fig. 2.—Case 1. Section of the left ventricle showing dense, fibrous, epicardial adhesions. No cellular infiltration of the myocardium is present.

1931. A cough, becoming worse four days before admission, had been present for several months. Chilly sensations were recently noted and sweating was frequent.

On admission, he was acutely ill, with rapid respirations. The right lung was clear but crackling râles were heard over the left axilla and the left infrascapular area. The heart was not remarkable. The abdomen was distended and the epigastrium tender. After some improvement, the temperature rose suddenly to 105° F. on March 19 and the temperature curve continued to be septic in type. Signs of increased pulmonary involvement were noted bilaterally, followed by evidence of fluid at the left base and axilla. On March 23, thoracentesis in the left axilla was unsuccessful. Because of pulsus paradoxus, an attempt was made to tap the pericardium. Through the fifth intercostal space in the anterior axillary line, 625 c.c. of creamy pus were removed. (Autopsy showed this pus to have come from an empyema and not from the pericardial cavity.) Death occurred March 24.

Pertinent laboratory data included cultures of hemolytic streptococci from the sputum and pleural exudate. A blood culture was sterile. The leucocyte count rose from 5,250 on admission to 19,400 on March 22. Blood Wassermann and Kahn tests were negative. For electrocardiograms, see Fig. 3.

Autopsy (No. 5515).—The autopsy was done fifty-seven hours after death. Anatomical Diagnosis: Lobular pneumonia and multiple abscesses of left lung. Septicemia—hemolytic streptococcus. Extensive edema and hemorrhages of both lungs. Fibrinopurulent exudate of left pleural cavity, pericardium, and epicardium —hemolytic streptococcus. Foci of subepicardial myocarditis. Small hemorrhages in spleen, lymph nodes, adrenals, and brain. Acute splenic tumor. Hyperplasia of lymph nodes, splenic tumor type. Hyperplasia of bone marrow. Acute glossitis. Scarring of pancreas and testes. Chronic prostatitis.

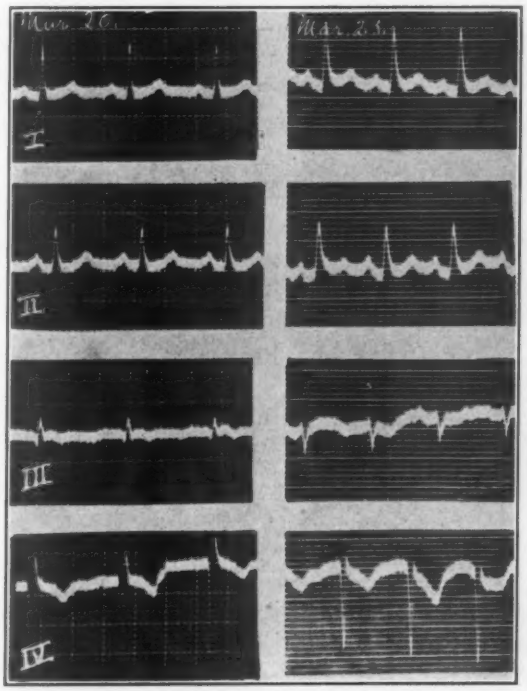

Fig. 3.—Case 2. Lobular pneumonia with empyema and early pericarditis (hemolytic streptococcus). The record of March 20 is not abnormal. That of March 23 shows an elevation of the R-T segments in Leads I and II, with slurring of the descending limb of the R-wave. A slight change in the axis deviation is apparent. No essential change is present in the chest lead.

Lungs.—Numerous small, soft, gray areas were scattered through both lobes of the left lung. These lesions, microscopically, were small abscesses surrounded by zones of lobular pneumonia. In both lungs were extensive areas of edema and hemorrhage and in the left pleural cavity were 250 c.c. of fibrinopurulent exudate.

Pericardium and Heart.—A thin layer of fibrinopurulent exudate on the outer surface of the pericardium was continuous with the pleural exudate. Only a thin layer of fibrin was present on the inner surface of the pericardium and on the epicardium, associated with not more than 40 c.c. of cloudy pericardial fluid. The heart weighed 310 gm. and, on section, the left ventricle was slightly dilated. The endocardium, valves, and coronary arteries showed no gross lesions.

Microscopically, a fibrinopurulent exudate was on the outer surface of the pericardium. Only small amounts of fibrin were present on the epicardium and on the inner surface of the pericardium, but both the pericardium and epicardium were heavily infiltrated with polymorphonuclear neutrophiles, lymphocytes, and mononuclear phagocytes. Where there was little epicardial fat; small numbers of polymorphonuclear neutrophiles, lymphocytes, and plasma cells were scattered about the superficial blood vessels and among the superficial muscle fibers of the myocardium (Fig. 4). In the sections from both auricles and ventricles, a few of the muscle fibers were necrotic. The deeper portions of the myocardium showed no microscopic lesions.

Bacterial Studies.—In post-mortem cultures of the blood from the heart and the pleural exudate, hemolytic streptococci and colon bacilli were grown. *Streptococcus viridans* and a colon bacillus were cultured from the left lung. With bacterial stains,

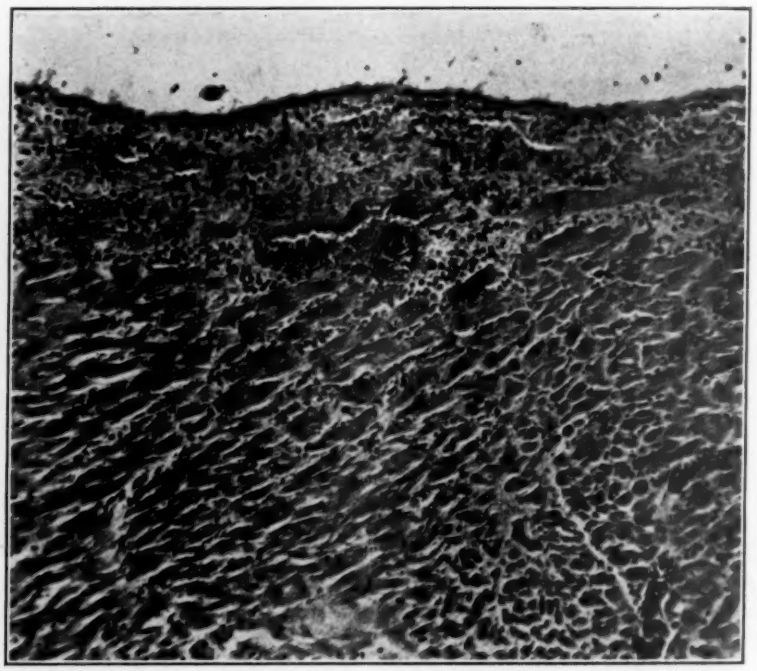

Fig. 4.—Case 2. Section of the left ventricle. The myocardium is invaded by the purulent epicardial exudate. The superficial muscle fibers are degenerating.

large numbers of gram-positive cocci in chains were seen in the pleural exudate and on both surfaces of the pericardium, but no organisms were found in the myocardium. Many gram-positive cocci were, likewise, present in the exudate of the left lung.

CASE 3.—(No. 39636.) T. A., a colored man, thirty-five years of age, was admitted to Medical Service A on Oct. 30, 1935, with a chief complaint of pain in the chest. He had had no serious illnesses and the family history was irrelevant. A cough had been present for several days, and following exposure to rain, he had had sharp pain of pleuritic type in the left lower chest. The cough was worse and shortness of breath was marked.

He was acutely ill on examination and perspired freely. Respirations were rapid and shallow. Signs of consolidation were present over the lower lobe of the left lung. The heart showed no abnormalities. The abdomen was distended and tender in the

left upper quadrant. Delirium was constant and the temperature remained at about 102° F. A marked pulsus paradoxus was noted on November 4, and he died on November 5.

Cultures of the sputum showed pneumococcus Type III, and a blood culture was positive for the same organism. The leucocyte count rose from 4,350 on November 1 to 28,000 on November 4. Blood Wassermann and Kahn tests were negative. For electrocardiograms, see Fig. 5.

Autopsy (No. 5390).—The autopsy was performed thirteen hours after death. Anatomical Diagnosis: Confluent lobular pneumonia of left lung, pneumococcus Type III. Extensive fibrinopurulent exudate in both pleural cavities. Patchy areas of atelectasis and edema of lungs. Marked fibrinopurulent exudate, with beginning organization, of pericardium and epicardium. Foci of acute subepicardial myo-

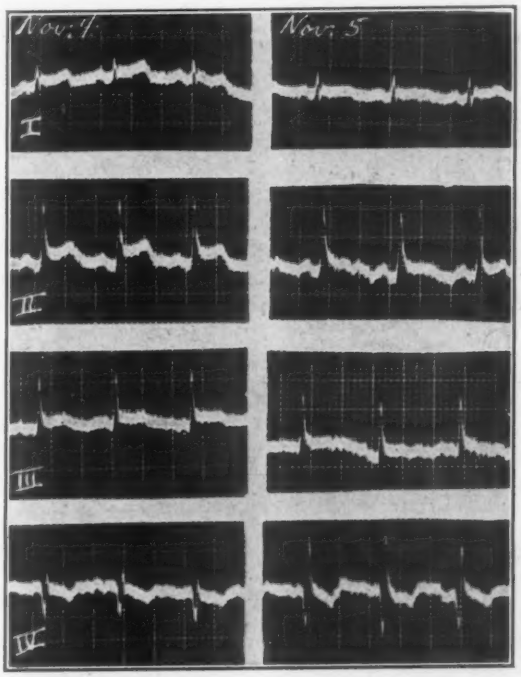

Fig. 5.—Case 3. Lobar pneumonia with bilateral empyema and fibrinopurulent pericarditis (pneumococcus). Note the elevation of the R-T segments in Leads I, II, and III of the electrocardiograms with no significant change in the chest lead.

carditis. Hyperplasia of peribronchial lymph nodes. Enlargement of axillary lymph nodes. Acute diaphragmitis. Hemorrhages in splenic pulp. Focal necroses in liver. Fatty changes of liver, slight. Small abscess in one kidney. Hyperplasia of bone marrow. Distention of stomach and intestines.

Lungs.—Confluent areas of gray consolidation, typical of pneumonia microscopically, were present in both lobes of the left lung. On the pleural surfaces of both lungs was a thick fibrinopurulent exudate. The left pleural cavity contained 500 c.c., and the right, 400 c.c. of cloudy fluid. The pleural exudate was continuous with a similar exudate on the external surface of the pericardium.

Pericardium and Heart.—The pericardium was thickened and indurated. A fibrinopurulent exudate was present on the internal surface and on the epicardium. About 400 c.c. of cloudy fluid were found in the pericardial sac. The heart with the

epicardial exudate weighed 410 gm. In many localities, for a distance of 2 or 3 mm. beneath the epicardium, the heart muscle was pale. The heart showed no other gross lesions.

Microscopically, the cells of the exudate on the pericardium and epicardium were predominantly polymorphonuclear neutrophiles many of which were necrotic. Both the pericardium and epicardium were edematous and heavily infiltrated with polymorphonuclear neutrophiles, mononuclear phagocytes, lymphocytes, and plasma cells. The small blood vessels were engorged and, in many areas, the fat was necrotic. In some localities, organization was occurring. Except where the epicardial fat was thick, the cellular infiltration reached the surface of the myocardium and extended into it for short distances about the blood vessels and superficial muscle fibers, which were pale-staining and frayed. Many of the nuclei of these fibers were pyknotic or vacuolated. Numerous small hemorrhages were present in the stroma. The deeper layers of the myocardium were normal in appearance.

Bacterial Studies.—At autopsy, blood culture from the heart showed numerous colon bacilli. Pneumococcus Type III was grown from the left lung. Large numbers of gram-positive cocci were stained in sections of the exudate from the lung, pleurae, pericardium, and epicardium. No organisms were seen in the myocardium.

CASE 4.—(No. 40463.) J. A., a colored male, fifty-seven years of age, was admitted to Medical Service B on Feb. 1, 1936. He complained of pain in the chest and left shoulder and shortness of breath. The family and past medical histories were not significant. He had been in good health until January 27, when he noted malaise and anorexia. He remained at home for three days, but returned to work on January 30, when he was seized with pain in the chest and cough productive of rusty sputum.

On admission he was acutely ill and respirations were rapid and shallow. The right middle and lower lobes were thought to be consolidated. The heart was enlarged to the left and the sounds were faint. The cardiac rate was 132, and the rhythm was totally irregular. A pulse deficit was noted. The abdomen was moderately distended. The left shoulder was swollen and painful on motion. The patient continued very ill, with a temperature sustained at 103° F. The cardiac rhythm was regular on February 2. A pericardial friction rub was present on February 4 and 5. On February 8 death occurred.

Significant laboratory data were as follows: pneumococcus Group IV was cultured from the sputum. On February 3, blood culture showed 100 colonies per c.c. of pneumococcus Group IV. On February 5, venous blood pressure was 8.8 cm. of water. Blood Wassermann and Kahn tests were negative. For electrocardiograms, see Fig. 6.

Autopsy (No. 5465).—The autopsy was done two hours after death. Anatomical Diagnosis: Lobar pneumonia of right lung. Septicemia, pneumococcus Group IV. Organizing fibrinopurulent exudate of right pleural cavity, pericardium, and epicardium, pneumococcus Group IV. Foci of acute subepicardial myocarditis. Acute phlegmonous abscess of left shoulder region. Swelling of left knee. Acute purulent meningitis, pneumococcus. Acute splenic tumor. Marked distention of intestines. Emphysema of lungs. Old fibrous pleural adhesions of left lung. Hypertrophy of left ventricle of heart. Hypertrophy of prostate. Extracapsular hyperplasia of cortical cells of both adrenals. Invasion of posterior lobe of hypophysis by basophile and chromophobe cells.

Body and Lungs.—The left shoulder was swollen and indurated and a deep phlegmonous abscess was found beneath the pectoral muscles in the axilla. A similar area of swelling about the left knee was not dissected. Scattered diffusely through the right lung were numerous small patches of lobular pneumonia. A thick fibrino-

purulent exudate, involving the pericardium, covered the pleural surface of the right lung and 350 c.c. of cloudy fluid were present in the pleural cavity. The left pleural sac was completely obliterated by dense old fibrous adhesions.

Pericardium and Heart.—The pericardium was thickened, gray, and opaque. On both the internal and external surfaces and on the epicardium was a fibrinopurulent exudate approximately 0.5 cm. in thickness. About 40 c.c. of cloudy fluid were present in the pericardial sac. The heart and epicardial exudate weighed 460 gm. On section, where there was little epicardial fat, the myocardium was pale for two or three mm. beneath the surface. The wall of the left ventricle was moderately thickened. No other gross abnormalities were noted.

Microscopically, the exudate on the surfaces of the pericardium and epicardium was composed of fibrin and disintegrating polymorphonuclear neutrophiles, into

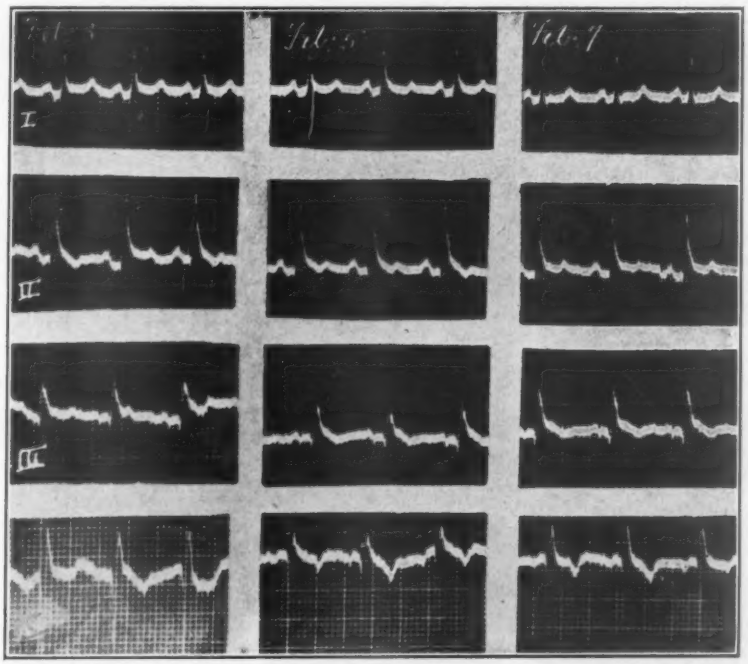

Fig. 6.—Case 4. Lobar pneumonia with empyema (right) and fibrinopurulent pericarditis (pneumococcus Type IV). Pericardial friction rub noted February 4. Death February 8. The first electrocardiogram shows an elevation of the R-T segments in Leads I, II and III, with slurring of the descending limb of the R-wave. The changes are greater in Leads II and III but no significant Q pattern is present. Return of the R-T segment to normal is seen in Lead I. The chest lead shows only slight R-T segment elevation in the record of February 5.

which fibroblasts and capillaries were growing. The pericardium and epicardium were heavily infiltrated with these cells and abscesses in the fatty tissue were numerous. Except where the epicardial fat was thick, the purulent exudate extended to the surface of the myocardium and moderate numbers of polymorphonuclear neutrophiles and round cells were present among the superficial muscle fibers (Fig. 7). Many of these fibers, particularly in the right ventricle, were pale-staining and the fibrils were broken or absent. Most of the nuclei were vacuolated (Fig. 8). A few of the most superficial fibers were necrotic. In the deeper layers of the myocardium, no such changes were present. The muscle fibers of the left ventricle were diffusely hypertrophied.

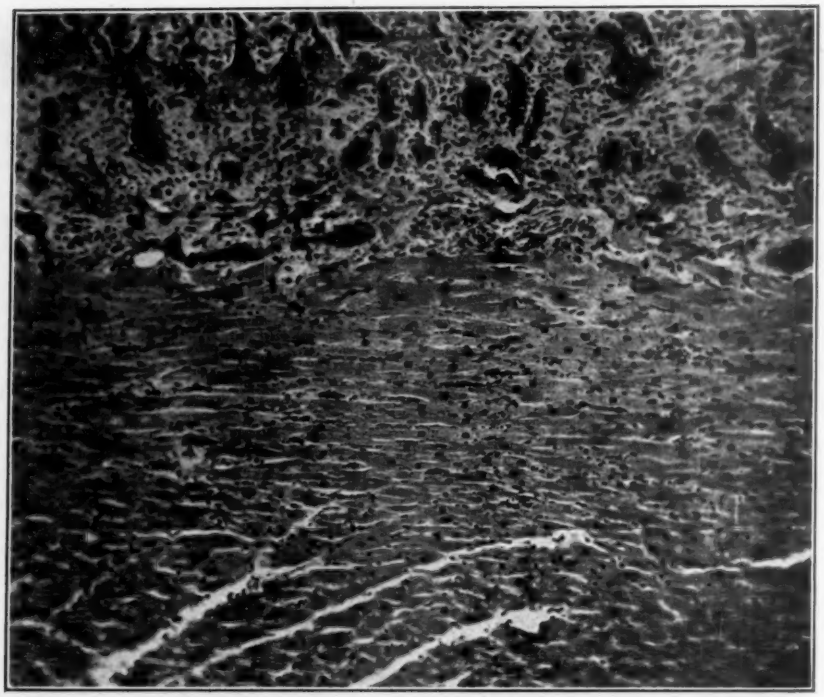

Fig. 7.—Case 4. Section of the left ventricle. The epicardial exudate is organizing. Leucocytes are scattered among the muscle fibers.

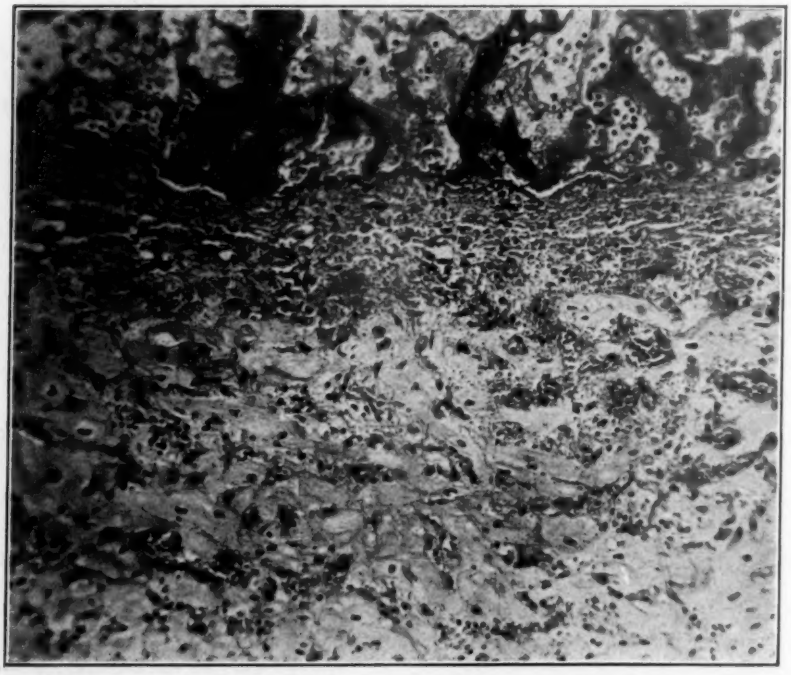

Fig. 8.—Case 4. Section of the right ventricle. The fibrinopurulent epicardial exudate is apparent. Leucocytic infiltration and degeneration of the myocardium is striking.

Bacterial Studies.—Pneumococcus Type IV was grown at autopsy in pure culture from the pericardial cavity. From the right lung only a bacillus of the colon group was cultured. In sections, occasional gram-positive cocci were seen in the pericardial and epicardial exudate, but none were found in the myocardium. Similar organisms were stained in the meningeal exudate. No bacteria were demonstrated in the pleural exudate, in the areas of pneumonia, or in the exudate of the left axilla.

CASE 5.—(No. 40278.) J. K., a white boy of eighteen years, was admitted to Surgical Service A on Jan. 13, 1936. He was in a critical condition from a stab wound in the third intercostal space 5 cm. to the left of the sternum. The pulse rate and blood pressure could not be determined and the heart sounds were inaudible. After emergency treatment for shock, the heart sounds were heard at a rate of 140 per minute. Less than two hours after admission, the patient was operated on by Dr. John B. Flick. The pericardium was tense and distended with blood.

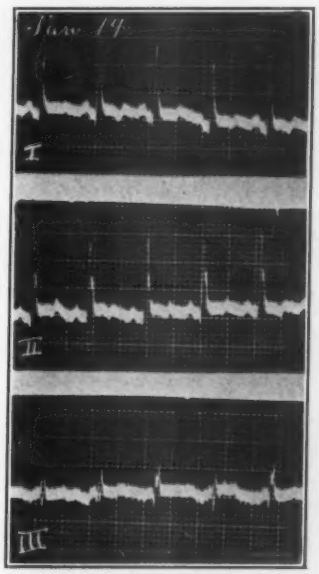

Fig. 9.—Case 5. Stab wound of right auricle. Death thirty-six hours after operation. Acute fibrinous pericarditis and lobular pneumonia. The electrocardiogram was taken about fifteen hours after operation. Note the elevation of the R-T segments in Leads I and II, with some slurring of the descending limb of the R-wave.

A laceration in the right auricle just above the auriculoventricular junction was sutured. During the operation the heart stopped beating, but contractions were resumed after massage of the ventricles. A transfusion of 1,100 c.c. was given on the operating table. After operation the blood pressure rose to 138/70.

The following day there was a fever of 102° F., considerable cyanosis, and a productive cough. The respirations were 48 per minute. The heart rate was 148 and the blood pressure 114/80. A definite pulsus paradoxus was noted. Dullness was present to percussion at the bases of both lungs, with crepitant râles on the right and bronchial breath sounds at the left infrascapular area. Because electrocardiographic changes were present and a bedside x-ray plate suggested enlargement of the cardiac shadow, paracentesis was attempted, but no blood or purulent fluid could be aspirated from the pericardial sac. The temperature, pulse, and respirations continued to rise and he died thirty-six hours after operation. For electrocardiogram, see Fig. 9.

Surgical Specimen (No. 22771).—The autopsy was performed on the day of death by a coroner's physician. Only a few blocks of tissue were allowed for study.

Heart.—A thick fibrinous exudate covered the epicardium and inner surface of the pericardium, but little fluid was said to be present in the pericardial sac. The sutured laceration in the right auricle was intact, but on the endocardial aspect of this lesion was a large mural thrombus. *Microscopically,* fragments of suture material were present in the right auricle and, on either side of the laceration, the myocardium was heavily infiltrated with polymorphonuclear leucocytes. Fragments of necrotic thrombus were attached to the endocardium. On the surface of the epicardium was a thick fibrinopurulent exudate. At some distance from the laceration, the entire wall of the right auricle was also infiltrated with polymorphonuclear neutrophiles, lymphocytes, and plasma cells. The muscle fibers were shrunken and the nuclei were pyknotic. In two sections of the left ventricle the epicardial fat

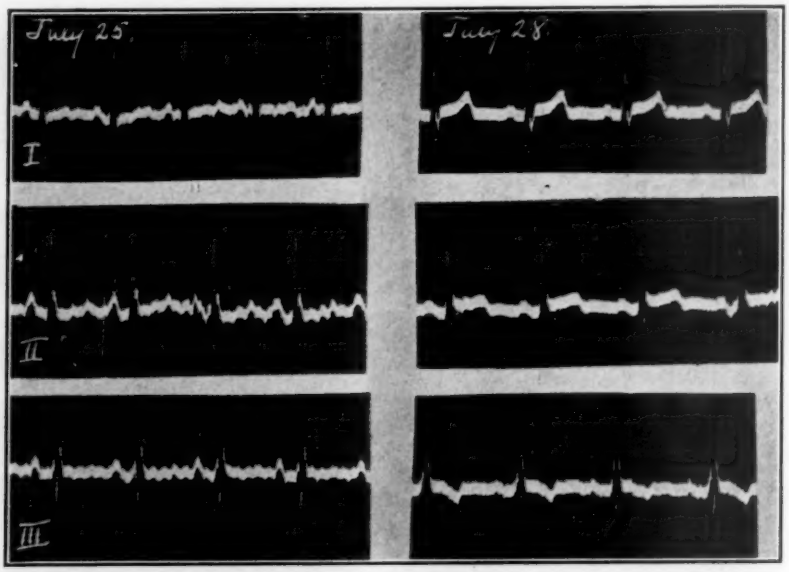

Fig. 10.—Case 6. Colored male aged forty-one years. Syphilitic aortitis with rupture into the pericardial sac. The first record was taken a few hours after admission because of agonizing chest pain and shock. It shows little of significance and no R-T segment change. The second record was taken about one hour before death. There is a slight but definite elevation of the R-T segments in Leads I and II, with inversion of the T-waves in Lead III.

was thick and the exudate did not reach the surface of the myocardium. The muscle fibers appeared normal. No other blocks were available. Large numbers of gram-positive cocci, resembling staphylococci, were stained in the exudate of the epicardium and auricular myocardium.

Case 6.—(No. 3594.) C. J., a colored male, forty-one years of age, was admitted to Medical Service A on July 24, 1931. He had been in good health until the evening of admission when he noted nausea and oppression in the chest. He became dizzy and lost consciousness. On recovery a few minutes later, he had agonizing pain in the chest, made worse by inspiration. He was rushed to the hospital and on arrival was in shock. The blood pressure was 90/60 and the pulse 130. He vomited repeatedly. Scattered fine and coarse râles were present over the lungs. The heart showed slight enlargement to the left but no murmurs or friction rub were heard.

The abdomen was not remarkable and the right leg had been amputated below the knee. A large chronic ulcer was present over the medial aspect of the left leg.

The following day an aortic diastolic murmur was heard and the lungs were clear. On July 27 enlargement of the cardiac dullness was noted on percussion, but the patient seemed generally improved. Death occurred suddenly on July 28 after an attack of acute dyspnea with rapid disappearance of the pulse.

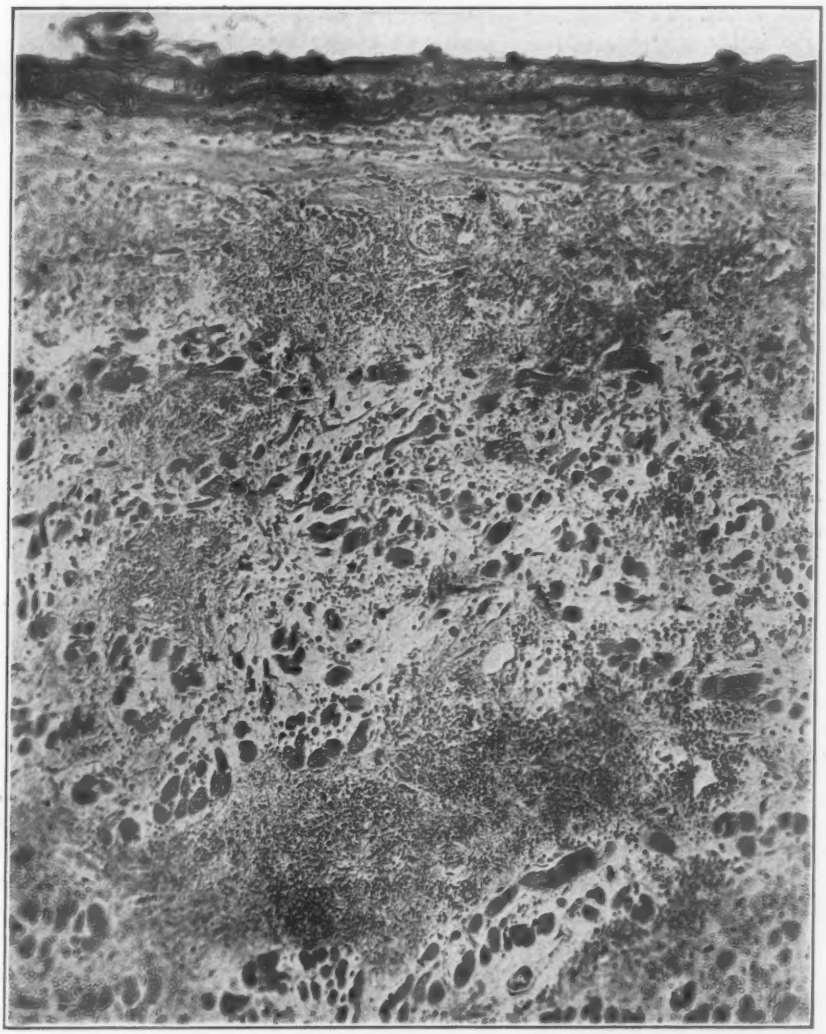

Fig. 11.—Case 6. Section of the right ventricle. The fibrinous epicardial exudate is scant. The hemorrhage and edema in the myocardium are marked. Many of the muscle fibers are degenerating or necrotic.

Laboratory data included strongly positive Wassermann and Kahn tests and slight leucocytosis. For electrocardiograms, see Fig. 10.

Autopsy (No. 4424).—The autopsy was done two and one-half hours after death. Anatomical Diagnosis: Syphilitic aortitis. Laceration of ascending arch of aorta with rupture into pericardial sac. Hemopericardium. Edema and hemorrhage of

pericardium. Acute fibrinous pericarditis. Foci of acute inflammation, hemorrhage, and edema in right ventricle of heart. Hypertrophy and dilatation of heart. Diffuse scarring of interventricular septum. Old tuberculous lesions in apex of right lung. Anthracosis, slight. Chronic ulcer of left leg. Absence of right leg below the knee.

Aorta.—Just above the ring of the aortic valve was a stellate laceration of the intima and media. Blood had extravasated through the adventitia into the pericardial cavity. In all portions of the arch, elevated fibrous plaques were present in the intima and the media beneath was grossly scarred. Microscopically, the lesions were typical of syphilitic aortitis. At the point of rupture, a large, fresh area of necrosis, associated with round cell infiltration, extended through the entire thickness of the media.

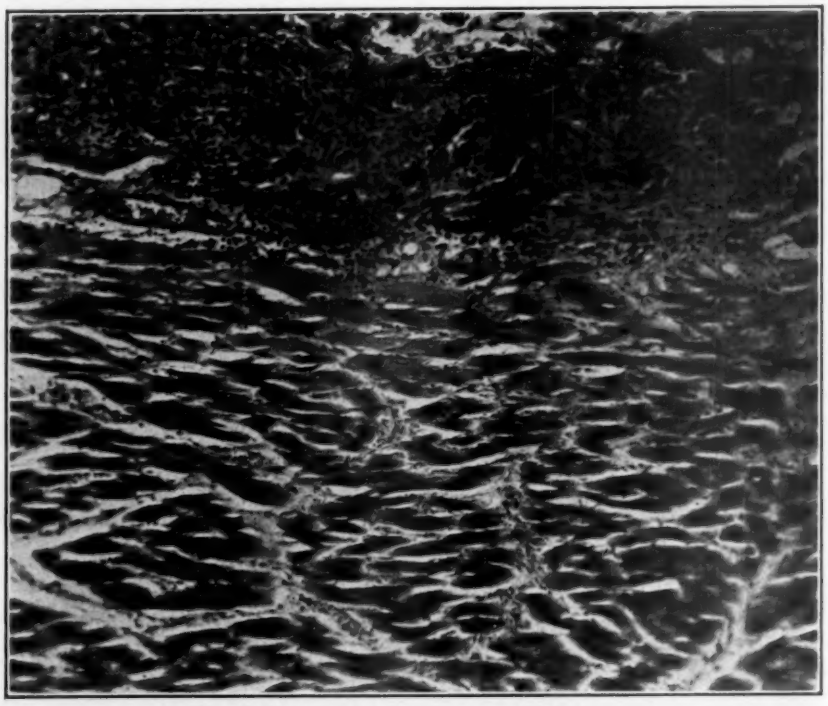

Fig. 12.—Section of the left ventricle from a case of uremic pericarditis. The epicardial exudate, composed largely of round cells, does not infiltrate the myocardium. The muscle fibers are hypertrophied.

Pericardium and Heart.—The anterior layer of pericardium was moist and bloody. The pericardial sac contained 750 c.c. of clotted blood. Thin layers of fibrin covered the epicardium and inner surface of the pericardium. The heart weighed 600 gm. The left ventricle particularly was hypertrophied and the wall measured 22 mm. in thickness. Small, firm, white streaks were visible beneath the endocardium in the interventricular septum. The endocardium, valves, and coronary arteries showed no lesions.

Microscopically, much of the fatty tissue in the pericardium was destroyed by fresh hemorrhage and edema. On the epicardium was a thin fibrinous exudate. In the areolar tissue were numerous hemorrhages and small collections of lymphocytes and plasma cells. Extravasated blood was present among the superficial fibers of

the left ventricle. The lesions in the right ventricle, however, were most marked. Hemorrhages, edema, and collections of round cells and polymorphonuclear neutrophiles were scattered through the entire wall. Many of the muscle fibers were necrotic or absent (Fig. 11). Except for moderate hypertrophy of the muscle fibers in the left ventricle and diffuse scarring in the interventricular septum, no other lesions were seen. No bacteria were stained in the epicardium or myocardium.

In three patients with active rheumatic heart disease, pericarditis was determined by friction rubs and roentgenographic studies in all cases. Serial electrocardiograms showed no significant RS-T changes. No deaths occurred.

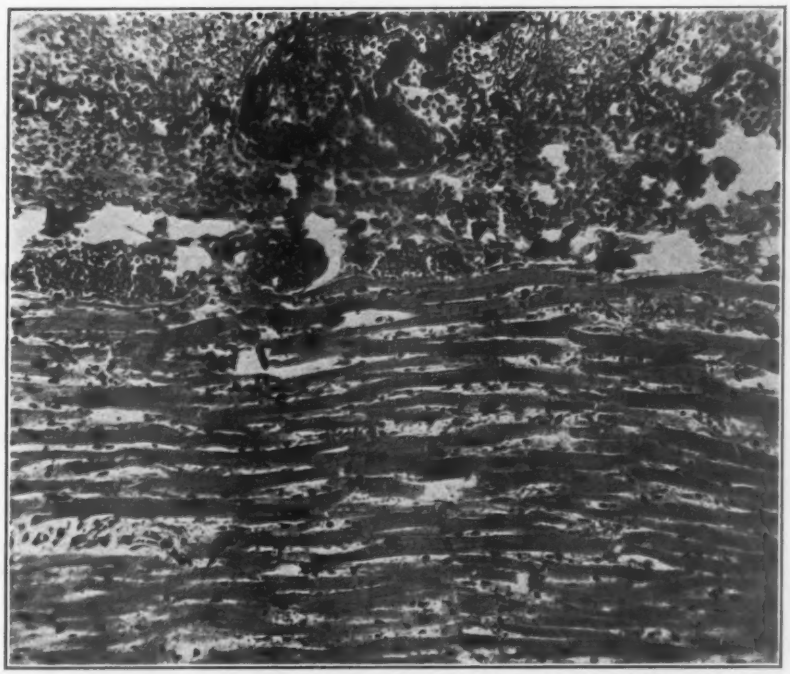

Fig. 13.—A section of the left ventricle from a case of pneumococcic pericarditis which showed no electrocardiographic changes. The fibrinopurulent epicardial exudate does not invade the myocardium and the muscle fibers are not degenerated.

Three patients with uremic pericarditis likewise showed no significant changes in the electrocardiograms. In the two cases examined at autopsy, extensive fibrinous pericarditis was present, accompanied by 60 c.c. and 300 c.c. of serous fluid. The inflammatory epicardial exudate did not invade the myocardium in many sections of both auricles and ventricles. The muscle fibers were hypertrophied but not degenerated (Fig. 12).

Two of the patients with lobar pneumonia and pericarditis had normal electrocardiograms. Marked fibrinopurulent pericarditis in both was associated with 40 c.c. and 350 c.c., respectively, of pericardial

fluid. Microscopically, the purulent exudate in the epicardium did not invade the myocardium in numerous sections from the auricles and ventricles (Fig. 13) except in three small areas in one case. No degenerative changes were seen in the muscle fibers.

DISCUSSION

In this study a direct chest lead was used in all but two of the patients. This lead was taken by placing the precordial electrode on the fifth left intercostal space in the midclavicular line and the indifferent electrode on the left leg (Lead V of Wolferth and Wood).

The electrocardiographic changes in five of seven cases of purulent pericarditis and in the case of hemopericardium are similar and seem characteristic enough to be of diagnostic value. The typical finding is elevation of the R-T segments in Leads I, II, and III, usually most marked in Lead II. Slurring of the descending limb of the R-wave frequently occurs. In four of the cases, these changes were primarily in Leads I and II and in two cases were mainly in Leads II and III. A definite Q-wave in Lead III was seen in only one case. In the four cases having typical electrocardiographic changes in which the chest lead was obtained, no significant abnormalities were seen in this lead.

The resemblance of electrocardiograms in pericarditis to those in acute myocardial infarction has been commented on in the literature. An electrocardiogram with no reciprocal action of the RS-T segment in Leads I and III and with the greatest elevation of the R-T segment in Lead II is not typical of either an anterior or posterior infarct. Because Lead II shows a summation effect of the changes in Leads I and III, myocardial infarction involving both the anterior and posterior surfaces of the left ventricle may produce changes of this type (i.e., elevation of the R-T segment in all leads, greatest in Lead II). In this combined infarction, however, a well-developed Q pattern or changes in the chest lead, or both, should be present. The electrocardiographic changes described in our cases, therefore, are not characteristic of any type of myocardial infarction.

Cardiac tamponade is the usual explanation given in the literature for the changes in the RS-T segment. In some patients, however, moribund with tamponade from hemopericardium, normal electrocardiograms have been obtained before operation.[1, 7] Of our six patients with "positive" electrocardiograms, three had no appreciable increase in the amount of pericardial fluid. Five patients with no electrocardiographic changes *had* increased amounts of pericardial fluid by x-ray films or at autopsy. Our first case, moreover, showed a return of the elevated R-T segments to normal while the amount of pericardial fluid was increasing (Fig. 1). In this small series of cases, therefore, we can see no relation between the amount of peri-

cardial fluid and electrocardiographic changes. The progressive electrocardiographic changes in many cases of stab wound of the ventricle[6, 7, 8] suggest acute pericarditis rather than a single anterior lesion of the myocardium. In our case of this type, the lesion was in the auricle and the changes in the ventricular complexes of the electrocardiogram could not have been caused by the stab wound.

In three of the cases with purulent pericarditis, microscopic study showed inflammatory and degenerative changes of the superficial myocardium. Where the epicardial fat was thick the underlying myocardium appeared normal. In Case 1, although groups of superficial muscle fibers appeared to have been replaced by scar tissue, no active inflammation was present in the myocardium. The two blocks from the left ventricle, in Case 4, were covered with thick layers of epicardial fat and the subjacent myocardium showed no lesions. Myocarditis was, however, present in the right auricle even at a distance from the line of suture. In Case 6, with hemopericardium, not enough blocks were available for study, but large areas of hemorrhage, edema, and cellular infiltration were present in the right ventricle. In the two cases of pneumococcic, and the two of uremic pericarditis, in which no electrocardiographic changes occurred, careful study showed no significant inflammatory changes of the myocardium. *It is, therefore, believed that the electrocardiographic changes reported are the result of superficial myocarditis.* Involvement of both the anterior and posterior surfaces of the ventricles would explain the summation effect of the R-T segment in Lead II. The absence of deeper myocardial damage might account for the lack of any well-developed Q-wave patterns or of significant changes in the chest lead.

If myocardial inflammation is present, it is probable that some cases of nonsuppurative pericarditis would show similar electrocardiographic changes. It is also likely that in some cases of purulent pericarditis electrocardiographic changes may be transient.

SUMMARY

1. Studies on fourteen cases of acute pericarditis are presented. Seven of these cases were purulent in type and six were serous. One followed hemopericardium.

2. Similar changes in the electrocardiograms were present in five of the seven cases of purulent pericarditis. Less marked changes occurred in the case of hemopericardium. In the remaining cases, such abnormalities were not found.

3. The characteristic electrocardiographic pattern consists of an elevation of the R-T segments in the three limb leads. This change is often most striking in Lead II. Slurring of the descending limb of the R-wave is frequent. A normal chest lead (apex of heart and left

leg), the absence of a reciprocal action of the RS-T segments in Leads I and III, and no well-developed Q pattern, differentiate this condition from acute myocardial infarction.

4. In this series of cases, we find no relation between the amount of pericardial fluid and electrocardiographic changes.

5. Microscopic study of the hearts in all cases with "positive" electrocardiograms showed definite subepicardial myocarditis. Autopsies were obtained in four cases with normal electrocardiograms. In none was the pericarditis associated with inflammation of the myocardium.

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THE CIRCULATION TIME OF THE BLOOD OF DOGS, DETERMINED BY IONIZATION (GEIGER COUNTER) METHODS

I. The Effects of Physicophysiological Agents and of Drugs

Earl C. McCracken, Ph.D.,* Hiram E. Essex, Ph.D., and Charles Sheard, Ph.D.
Rochester, Minn.

THE circulation time of the blood between two chosen points in the body may be defined as the time between the injection of a substance at one point and the detection or registration of its arrival at the second point by means of its color, vasodilator or vasoconstrictor effects, neuromuscular stimulation, effects on the electrical properties of the blood, fluorescence, or radioactive qualities. In our investigations the time of circulation of the blood of dogs was measured between a point in the jugular vein and a point in that portion of the superficial femoral artery lying in the adductor canal. The ensemble of apparatus which was used is a modification suggested by the researches of Blumgart[1] and his colleagues. Essentially the apparatus consists of: (1) an ionization chamber, often referred to in the literature of physics as the Geiger counter; (2) a source of high voltage (approximately 2,500 V.) for the ionization chamber; (3) three stages of amplification with their own power supplies; and (4) a mechanism for recording the receipt of ionizing energy or changes in ionization in the Geiger chamber. Details concerning the ensemble of apparatus and its modus operandi are to be found in a communication published elsewhere.[2]

The radioactive material used as the ionization agent consisted of 1 to 2 c.c. of a solution containing the disintegration products obtained from 3 to 5 millicuries of radon (radium emanation). The most active constituent in this solution from the standpoint of gamma radiation is radium C, which has a half period of about twenty minutes and changes to radium D. In two to three hours the activity of the injected radioactive material decayed sufficiently to permit the use of the same animal in other tests during the day.

The procedure in determining the circulation time of the blood consisted in the proper placement of the ionization chamber over the superficial femoral artery, the injection of the radioactive material into the jugular vein, the automatic recording (on an apparatus carrying a strip

From the Division of Physics and Biophysical Research and the Division of Experimental Surgery and Pathology, The Mayo Foundation and the Mayo Clinic.
*Fellow in Biophysics, The Mayo Foundation; now Associate in the Department of Physics, Iowa State College, Ames, Iowa.

of paper moving at a uniform and known rate) of the time which elapsed between injection and arrival of active material under the aluminum window of the ionization chamber. Figure 1 is a reproduction, on a reduced scale, of a typical record. Since the speed of the paper on which records were made is known, it is possible to convert the recorded distance between the period of injection and arrival of radioactive material into the time of circulation of the blood between the two points.

This method and procedure are particularly advantageous in investigations of this character because there is: (1) lack of trauma, (2) deletion of reaction periods, (3) the ability to use trained animals, (4) the possibility of using the same animal repeatedly, and (5) immediate and positive detection of the arrival of the injected material.

THE CIRCULATION TIME OF THE BLOOD UNDER BASAL CONDITIONS

The circulation time of the blood (using trained dogs) between the jugular vein and the superficial femoral artery lying in the adductor canal was taken to be its basic value when the animal, after a twenty-

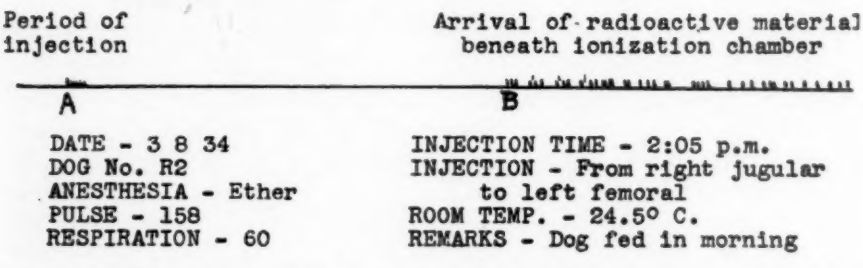

Fig. 1.—Reproduction of an original record (reduced approximately a third). The circulation time of the blood in this case is 6.5 seconds as determined from the time of passage of the radioactive material from the jugular vein (*A*) to the receipt of the active material in the femoral artery (*B*).

four-hour fast, was under conditions of complete rest on the table, with a pulse rate which was constant for at least five minutes. Under these conditions there were variations in the circulation time of the blood of each dog. For purposes of comparison in other portions of these investigations, a basic normal circulation time was determined for each dog by averaging a considerable number of values obtained for the time of circulation. Table I is a compilation of values of basic normal circulation time and germane data. These basic circulation times ranged from 6.75 to 15.6 seconds for the various dogs used. The data (recorded in part in Table I) show that there is no apparent relationship between the time of circulation of the blood and age, sex, physical condition, or weight of the animals. In contrast, however, the data show that the number of heartbeats which occurred during a specified time of circulation was very nearly the same in all dogs, irrespective of the wide differences in circulation time. The range of values of heartbeats per circulation time was between 13.0 and 16.38; the average value is 14.5 heart-

beats per circulation time. Further investigations are in progress concerning the possibility of establishing a relationship between pulse rates and circulation times to the end that, under the criteria stated, the time of circulation between the points specified may be empirically determined.

TABLE I

BASIC NORMAL CIRCULATION TIME

DOG	WEIGHT, KG.	NUMBER OF DETERMINATIONS	RANGE OF NORMAL CIRCULATION TIME (JUGULAR VEIN TO FEMORAL ARTERY), SEC.	BASIC NORMAL CIRCULATION TIME, SEC.	RANGE OF PULSE RATE, PER MIN.	BASIC NORMAL PULSE RATE, PER MIN.	HEARTBEATS PER CIRCULATION TIME
1	16.0	3	12.0 to 15.0	13.53	56 to 64	60.0	13.5
2	7.5	8	9.0 to 13.0	11.25	66 to 80	71.5	13.4
3	17.0	9	12.0 to 16.5	14.05	54 to 72	59.0	13.0
4	17.0	4	6.0 to 8.0	6.75	104 to 120	116.0	13.05
5	16.5	3	9.0 to 12.5	10.83	67 to 87	78.0	14.1
6	17.0	5	14.0 to 17.5	15.6	58 to 70	62.0	16.1
7	15.0	4	9.5 to 12.5	11.1	78 to 90	84.0	15.45
8	12.0	4	9.5 to 13.0	11.5	80 to 90	85.5	16.38
9	14.0	3	7.0 to 10.0	8.0	100 to 106	102.0	13.6
10	12.0	3	7.0 to 10.0	8.5	102 to 117	109.0	15.5

EFFECTS OF VARIOUS PHYSICOPHYSIOLOGIC AGENTS ON THE CIRCULATION TIME

Exercise.—The results of our experiments show that the time of circulation was decreased very markedly immediately after exercise (one to two hours on a treadmill traveling at 1.7 miles per hour), the decreases ranging from 36 to 48 per cent of the control (normal basic) values. Computed from the standpoint of changes in velocity, the range of decrease was from 56 to 95 per cent. These findings are in close agreement with the range of changes in the pulmonary velocity obtained by Ellis.[3] The increase in pulse rate nearly paralleled the changes in velocity, as is evidenced by the fact that the number of heartbeats per circulation time remained approximately the same (within 10 to 15 per cent) as in the normal basic conditions. The fact that the number of heartbeats per circulation time was reduced in every case would lead to the inference that, during exercise, not only the pulse rate but also the stroke output increased.

Effects of Low Environmental Temperatures.—During the winter months several of the dogs used in this series of investigations were removed from an enviroment of 25° C. and placed for an hour or more outdoors at a temperature below 0° C. A sample set of data is: at a room temperature of 25° C., the pulse rate was 60 per minute and the circulation time of the blood 14.1 seconds; after being outdoors and subsequently removed to a room temperature of 17° C., the pulse rate was

79 and the circulation time 12.0 seconds; normal basic heartbeats per circulation time were 14; after being in the cold environment, 15.8. Our data show that the number of heartbeats per circulation time was increased subsequent to being in the cold environment, the average percentage increase (12.6 per cent) being slightly higher in value than the average percentage decrease (10.4 per cent) after exercise.

Effects of High Environmental Temperatures.—Each of the dogs was subjected to measurement under environmental temperatures of 29, 37.5, and 41° C. (± 1° C.), respectively. In each instance the animal remained on the observation table in the room at the specified temperature for nearly two hours prior to the determination of the circulation time. We found that there was no significant change in the circulation time of the blood unless the body temperature of the animal rose above normal values (approximately 39° C.). Under these conditions, with a rise of body temperature of about 1° C., the pulse rate increased markedly and there was a very decided decrease in the circulation time. When placed in an environmental temperature of 40° C., the increases in the pulse rates of two dogs were 22 and 55 per cent respectively, whereas the decreases in circulation time were 32 and 47 per cent. The number of heartbeats per circulation time remained practically constant, ranging from 15.5 to 16 in one dog and from 16.4 to 16.8 in the second dog.

DRUGS WHICH DECREASE THE CIRCULATION TIME

The general procedure for testing the effects of various drugs on the circulation time was the same in all cases. The normal basic circulation time was determined, followed by an interval of two to three hours to allow the disintegration products of the injected radioactive material to decay to values which did not produce responses in the Geiger chamber. The drug was then injected and, after a predetermined period of time (which varied for the different drugs used), another portion of the radioactive solution was introduced through the same needle, and the time of circulation of the blood determined. The administration of thyroxin, histamine, and ether anesthesia decreased the circulation time in the order named; increases in circulation time were produced by cobefrin, epinephrine, nicotine, pitressin, and pituitrin, respectively, in the sequence stated.

Thyroxin.—The basic circulation time of the blood of each of the dogs used was determined. Each animal was then given 1 c.c. of a (1 mg. per c.c.) solution of thyroxin per kilogram of body weight on two successive days. The circulation time was determined on the third day. Marked reductions in the values of the circulation time were found; the percentage decreases ranged from 21 to 51 per cent. Such decreases in circulation time are in conformity with the increases of minute volume blood flow in the femoral artery of a dog after feeding of desiccated

thyroid gland as found by Herrick, Essex, Mann, and Baldes.[4] A fairly uniform decrease in the number of heartbeats per circulation time was evident in all cases, the decrease ranging from 16 to 25 per cent.

Histamine.—The radioactive solution was injected one minute after the injection of 1 mg. of histamine. In all cases there was a marked increase (ranging from 60 to 95 per cent) in the pulse rate and a corresponding decrease (ranging from 110 to 40 per cent) in the time of circulation of the blood subsequent to the injection of the drug. The number of heartbeats per circulation time was increased (about 10 per cent) in two dogs and decreased in two other animals.

Ether.—Ether anesthesia was maintained by the auto-inhalation method; the depth of anesthesia was that which is commonly spoken of as "surgical" ether anesthesia. Sheard, Rynearson, and Craig,[5] by measurements of the temperature changes of the extremities, and Herrick, Essex, and Baldes,[6] by direct determinations of changes in blood flow, demonstrated that surgical ether anesthesia is nearly, if not equally, as effective in producing vasodilatation of the blood vessels of the dog as sympathectomy. It was of interest, therefore, to determine the change in circulation time produced by this agent. In every case (4 dogs) the circulation time was decreased, the percentages of decrease ranging from 21.5 to 54.5. The pulse rates increased within the range of 120 per cent to nearly 200 per cent. The number of heartbeats per circulation time was increased within a range of 13.5 to 57 per cent.

DRUGS WHICH INCREASE THE CIRCULATION TIME

Epinephrine (cobefrin).—In every case 1 c.c. of 1:1000 solution of epinephrine or the equivalent strength of cobefrin per kilogram of body weight was administered prior to the injection of the radioactive material, the same needle being used for the two injections. A series of controlled experiments, injecting equivalent dosages of epinephrine or cobefrin (concentration fivefold as great as epinephrine) into the same animal, were carried out under similar conditions of time of injection of drug previous to the introduction of the ionizing agent. No differences in the effects of the two drugs or the time of circulation of the blood could be detected.

The circulation time of the blood and the number of heartbeats per circulation time are markedly affected by the period of time intervening between the injections of the epinephrine and of the ionizing agent used for the determination of the circulation time. The results obtained in the case of a dog having a basic normal circulation time of 8.5 seconds and basic normal pulse rate of 109 per minute subsequent to intervals of 30, 60, 90, 120, 180, and 240 seconds between intravenous injection of epinephrine (0.11 c.c. in each instance) and the determination of the circulation time, are shown in Fig. 2. Data of a similar character were

obtained from experiments on other dogs. The maximal increase in circulation time (from 8.5 to 26 seconds, Fig. 2) was obtained sixty seconds after the injection of epinephrine. The time of circulation of the blood returned to its basic value about 120 seconds after injection of the drug, no appreciable changes in the circulation time occurring at intervals of 180 and 240 seconds after the injection. In brief, the circulation time of the blood is increased over 200 per cent, the pulse rates are decreased about 10 per cent (for example, from 109 to 96 per minute) and the number of heartbeats per circulation time is increased 200 per cent at 60 seconds after injection. The curve (dotted line, Fig. 2) correlating the number of heartbeats per circulation time and the

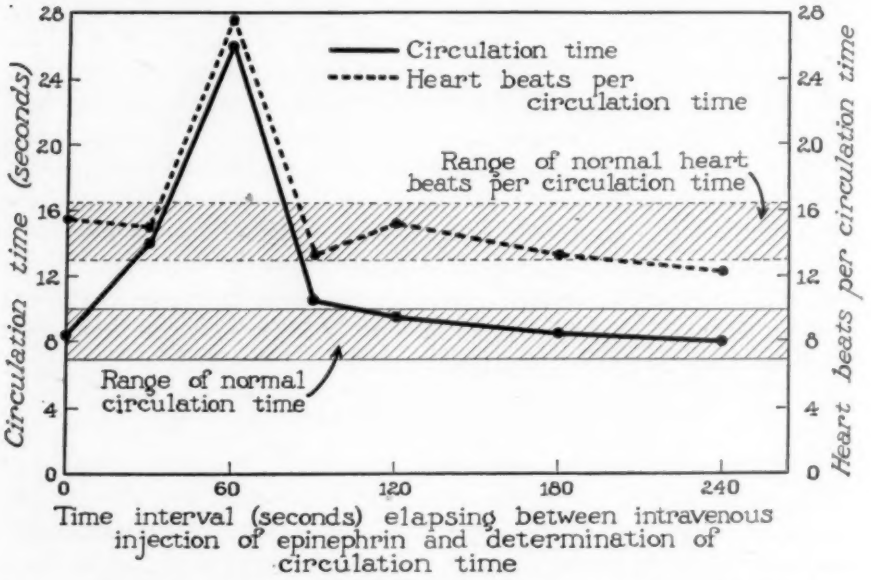

Fig. 2.—Curves showing the relationships between the circulation time of the blood in seconds, the number of heartbeats per circulation time and the periods of time after the injection of epinephrine.

period of time elapsing after the injection of epinephrine practically parallels the course of the curve of circulation time.

Various controversies have arisen concerning the action of epinephrine; some investigators have reported increased circulation times while other workers have obtained decreases. In none of our observations have we found any indication of a speeding-up of the circulation between the jugular vein and right femoral artery after the intravenous administration of epinephrine in dogs.

Nicotine.—In two dogs, in which the time elapsing between the injection of the nicotine and the radioactive material was short, namely, 15 and 8 seconds, there was an increase of the circulation time of 48 (from 11.5 seconds to 17 seconds) and 78 (from 9 seconds to 16 seconds)

per cent, respectively. In two dogs higher pulse rates were recorded (73 and 78 per cent), whereas in the other two animals decreased pulse rates (31 and 26 per cent) were noted. In all instances the number of heartbeats per circulation time was increased, the increase ranging from 23 (for example, 7.8 to 9.5 heartbeats) per cent to 314 (for example, 14 to 58 heartbeats) per cent.

Pituitrin and pitressin.—Intravenous injections of these drugs, in dosages (0.2 to 0.5 mg.) somewhat higher than those therapeutically administered to man, were made 60 or 90 seconds prior to the injection of the radioactive material. A very large increase in the circulation time was observed in all animals. On account of the marked vasoconstrictor action of these drugs, it was difficult to determine accurately the time of arrival of the radioactive material. The increases in circulation time ranged from 125 to 400 per cent after the injection of pituitrin, and from 285 to 510 per cent after the injection of pitressin. The difference between the ranges for the two drugs is not to be considered as significant because of the difficulty of obtaining and interpreting the records. The number of heartbeats per circulation time was increased; the ranges of increase were 135 to 170 per cent for pituitrin and 100 to 175 per cent for pitressin. Geiling, Herrick, and Essex[7] have shown that there is a marked decrease in the minute volume blood flow in the femoral and carotid arteries of the dog after injections of either pituitrin or pitressin.

COMPILATION OF DATA ON THE SAME DOG

We were fortunate enough to be able to carry two or three dogs through the whole series of experiments. Table II contains the data

TABLE II

COMPILATION OF DATA CONCERNING CIRCULATION TIME OF THE BLOOD AND NUMBER OF HEARTBEATS PER CIRCULATION TIME AFTER THE USE OF VARIOUS PHYSICOPHYSIOLOGIC AGENTS AND DRUGS IN THE SAME DOG

DECREASE OF CIRCULATION TIME			INCREASE OF CIRCULATION TIME		
AGENT OR DRUG	CIRCULATION TIME, SEC.	HEARTBEATS PER CIRCULATION TIME	DRUG	CIRCULATION TIME, SEC.	HEARTBEATS PER CIRCULATION TIME
Normal	16.5	15.5	Normal	16.5	15.5
Chilling	12.0	15.8	Cobefrin	23.0	23.0
Exercise	10.5	12.0	Epinephrine	26.0	21.7
Thyroxin	11.0	12.4	Nicotine	38.5	29.5
Histamine	8.5	17.4	Pitressin	76.0	38.0
Ether	8.0	22.0	Pituitrin	86.0	37.3

concerning the normal basic circulation time of the blood and number of heartbeats per circulation time before and after the administration of the various physicophysiologic agents and drugs cited.

CONCLUSIONS

Using well-trained dogs, lying at rest on the table for about an hour prior to test and subsequent to a twenty-four-hour fast, we believe that our findings show that:

1. Injection of the rapid disintegration products of radon (radium emanation) at one point in the circulatory system and the detection of their arrival at another point in this system by means of an ionization chamber (Geiger counter apparatus) and amplifying system is a very accurate method for determining the circulation time of the blood.

2. There is a wide variation in the circulation time of the blood between the jugular vein and femoral artery in the various dogs, in the basal state, used in these investigations. There are also considerable variations in the individual basal circulation times.

3. There is no relationship between the circulation time of the blood and age, sex, physical condition, or weight of dog.

4. The number of heart beats per circulation time between the jugular vein and femoral artery tends to be the same in all dogs.

5. Exercise and placing in low environmental temperatures decrease the circulation time of the blood as well as slightly decreasing the number of heartbeats per circulation time.

6. Increase of environmental temperature does not alter the circulation time until the rectal temperature rises above its normal value. When this temperature is exceeded, the circulation time is markedly decreased with little, if any, change in the number of heartbeats per circulation time.

7. The administration of thyroxin (1 mg. per kilogram of body weight per day for two days prior to test) produces a decrease in circulation time.

8. Histamine and ether anesthesia produce a marked decrease in circulation time.

9. Nicotine, pituitrin, and pitressin cause marked increases in the circulation time and a large increase in the number of heartbeats per circulation time.

10. Epinephrine and cobefrin in equivalent dosage produce the same effect on the circulation time and the number of heartbeats per circulation time.

11. After the injection of epinephrine, the circulation time of the blood increases to a maximal value at sixty seconds, returns to normal values after two minutes and remains in the normal range thereafter.

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THE CIRCULATION TIME OF THE BLOOD OF DOGS, DETERMINED BY IONIZATION (GEIGER COUNTER) METHODS

II. The Effects of Digestion

Earl C. McCracken, Ph.D.,* Hiram E. Essex, Ph.D., and Charles Sheard, Ph.D.
Rochester, Minn.

THE ensemble of apparatus used and methods followed for obtaining the circulation time of the blood are described in another communication.[1] In brief, the procedure consists in the injection of a solution containing small quantities of the disintegration products of radon (radium emanation) into the jugular vein and obtaining the time of passage of the radioactive substance between the jugular vein and the femoral artery lying in the adductor canal, by the use of an ionization (Geiger counter) chamber.

The circulation time (in seconds) of the blood between the two specified points and the pulse rate per minute were determined after the animal had been fasted for twenty-four to one hundred ninety-two hours. Observations previously made during investigations on the circulation time of the blood demonstrated that the injected radioactive material did not decay to values sufficiently low to permit the use of the dog for further tests until two or three hours had elapsed, hence the number of determinations of the circulation time is limited to three in each working day. Subsequent to the determination of the basic circulation time following the period of fasting, the dog was allowed to remain at rest for about two and one-half hours, after which it was returned to the observation table and fed a meal consisting of 1 gm. of glucose for each kilogram of body weight, and from two to four eggs in 400 to 600 c.c. of milk (depending on the weight of the animal); or, in certain cases, a meal was made of meat and cereal. After completion of feeding, pulse rates were taken and closely followed until the rate had increased considerably above that which was obtained before the ingestion of food. When it was found that the increased pulse rate was maintained quite constant for a period of ten or more minutes, a second determination of the circulation time was made.

Data concerning the circulation time of the blood before and during the digestion of food, pulse rates, and types of meal ingested are

From the Division of Physics and Biophysical Research, and Division of Experimental Surgery and Pathology, The Mayo Foundation.
*Fellow in Biophysics, The Mayo Foundation. Now Associate in the Department of Physics, Iowa State College, Ames, Iowa.

TABLE I

EFFECTS OF DIGESTION ON THE CIRCULATION TIME OF THE BLOOD

DOG	WEIGHT, KG.	LENGTH OF FASTING, HR.	CIRCULATION TIME BEFORE FEEDING, SEC.	PULSE RATE BEFORE FEEDING, PER MIN.	TYPE OF MEAL*	TIME OF FEEDING TO INJECTION, MIN.	CIRCULATION TIME AFTER FEEDING, SEC.	PULSE RATE AFTER FEEDING, PER MIN.	HEARTBEATS PER CIRCULATION TIME BEFORE FEEDING	HEARTBEATS PER CIRCULATION TIME AFTER FEEDING	INCREASE IN PULSE RATE AFTER FEEDING, %	DECREASE IN CIRCULATION TIME AFTER FEEDING, %
1	7.5	24	9.0	80	1	70	6.5	91	12.0	9.85	13.7	27.8
		48	17.0	52	1	80	12.0	86	14.7	17.2	65.5	29.4
		120	13.5	56	2	220†	10.5	76	14.8	13.3	15.1	22.2
2	17.0	24	14.5	56	1	30	12.5	64	13.5	13.3	14.0	12.9
		24	13.5	60	2	50	11.0	70	13.5	12.8	16.6	18.5
		48	15.0	52	1	35	11.5	72	13.5	12.8	36.5	18.5
		48	16.5	48	2	62	13.5	60	13.2	13.5	25.0	18.2
		120	14.5	57	1	43	12.5	68	13.5	14.2	19.3	12.9
3	16.0	48	16.0	56	1	28	11.0	96	14.9	17.6	71.5	31.2
		48	17.1	50	2	48	12.1	84	14.15	16.8	68.0	29.4
4	17.0	48	7.0	104	1	32	5.5	110	12.1	10.1	5.7	21.4
		96	10.0	86	1	48	7.5	114	14.3	14.3	32.6	25.0
5	16.5	48	12.0	64	1	108†	8.0	96	12.8	12.8	50.0	33.3
		192	11.0	74	1	60	7.5	100	13.6	12.5	35.0	31.8
6	17.7	72	18.0	60	1	64	11.5	68	18.0	13.0	13.3	36.1
7	20.0	48	20.0	86	1	99†	14.5	125	28.6	30.2	45.3	27.5
8	14.0	24	15.0	106	1	115†	12.0	128	26.5	27.7	20.0	20.0
9	17.0	48	27.5‡	42	1	45	15.1	80	19.25	20.0	90.5	45.4

*Type of meal: (1) milk, egg, glucose; (2) meat and cereal.
†Injection made at the time of maximal volume flow of blood per minute.
‡Left saphenous vein to right femoral artery.

given in Table I. In toto, these investigations demonstrate that the circulation time of the blood in dogs which have been fasted for twenty-four or more hours is decreased 12.9 to 45.4 per cent during the course of digestion (presumably at its maximal point as judged by the highest rate of pulse). At first glance it might appear that there is a greater decrease in the circulation time after a forty-eight-hour fast than after a twenty-four-hour fast. An average of the data for the eight dogs used indicates an additional reduction of about 7 per cent in the circulation time after a forty-eight-hour fast. In the same dog, however, the circulation time is practically the same subsequent to the two periods of fasting. On the other hand, the percentage decrease in circulation time appears to be significantly less after a one-hundred-twenty-hour fast as compared to the results after a fast of twenty-four or forty-eight hours.

A comparison of pulse rates with time of circulation shows that, after a twenty-four-hour fast, the percentage decrease in circulation time was approximately the same as the percentage increase in pulse rate. In eight of the nine dogs subjected to a forty-eight-hour fast the percentage decreases in circulation time were very much less than the percentage increases in pulse rate. No apparent relationship exists between the two when longer periods of fast were given.

An inspection of the data relative to the number of heartbeats per circulation time shows that there were increases (average per cent increase, 9.2) in eight instances, decreases (average per cent decrease, 11.5) in eight, and no changes in two instances. There is evidence of a definite tendency for the number of heartbeats per circulation time in an individual dog to remain constant and of approximately the same value before and throughout the cycle of digestion, as well as under the influence of such physicophysiologic agents as exercise and changes in environmental temperature. In contrast, the number of heartbeats per circulation time is markedly affected by various drugs and by ether anesthesia.[2]

SIMULTANEOUS MEASUREMENTS ON MINUTE VOLUME FLOW AND CIRCULATION TIME OF BLOOD

Using the Herrick and Baldes[3] modification of the Rein[4] thermostromuhr, we were able to conduct a short series of experiments in which simultaneous measurements of the circulation time (seconds) and rate of volume flow of blood (c.c. per minute) were obtained. In these experiments, the diathermy-thermo-element was placed on the right femoral artery in the adductor canal; the time of receipt of the radioactive material in the left femoral artery, subsequent to injection in the jugular vein, was recorded. By reason of the fact that the radioactive deposits introduced into the body have not sufficiently decayed to permit frequent determinations of circulation time, simultaneous measurements

by the two methods were limited to (1) normal fasting conditions, (2) the height of digestion, and (3) three or four hours after the second set of simultaneous measurements of blood volume flow and circulation time. The height of digestion was based on the determination of the maximal rate of volume flow through the femoral artery as measured by the thermostromuhr method.

Figure 1 gives graphically the relations existing between the rate for one of the dogs in which data were obtained simultaneously by the two experimental methods. Subsequent to a forty-eight-hour fast, the circulation time was found to be 20 seconds (Fig. 1, point *a*, curve 1), the volume blood flow 140 c.c. per minute (curve 2) and the pulse rate 86 per minute (curve 3). The circulation time decreased to 14.5 (point

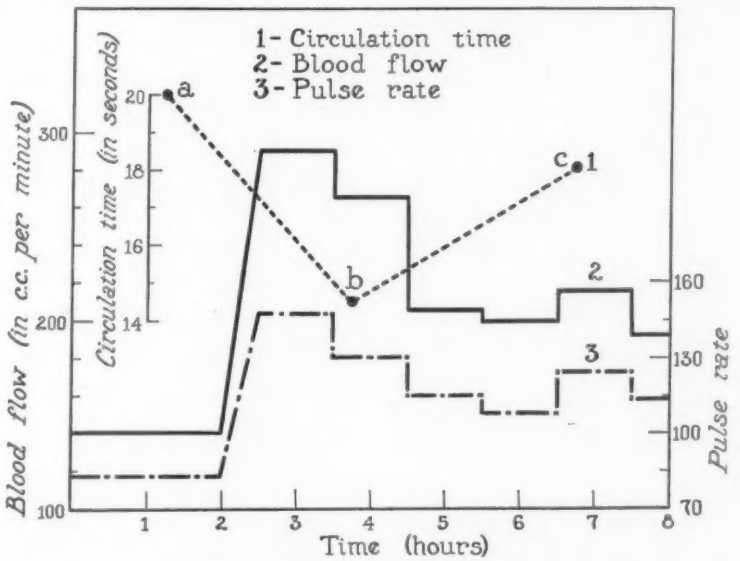

Fig. 1.—Relations between the circulation time of the blood, minute volume blood flow and pulse rate before, and subsequent to, the ingestion of food.

b, curve 1) after the ingestion of a milk-egg-glucose meal and at the time the minute volume blood flow was at, or near, its maximal value of 280 c.c. per minute, with a maximal pulse rate of 150 per minute. Three hours later the circulation time of the blood increased to 17.6 seconds (point *c*, curve 1), the pulse rate dropped to 128 per minute and the volume rate of flow decreased to 160 c.c. per minute. These curves and other sets of data (Table II) demonstrate that increases in the volume flow of blood were coincident with decreases in circulation time.

Our investigations corroborate the findings of Herrick, Essex, Mann, and Baldes[5] to the effect that the type of food ingested influences the time of onset and the duration of increased blood flow and pulse rate. Under similar conditions and using the same dog, the maximal increases

TABLE II

CIRCULATION TIME OF THE BLOOD (FROM JUGULAR VEIN TO FEMORAL ARTERY), VOLUME BLOOD FLOW (C.C. PER MINUTE), AND PULSE RATES PER MINUTE DURING THE DIGESTIVE CYCLE. MILK-EGG-GLUCOSE MEAL

DOG	WEIGHT, KG.	CIRCULATION TIME, SEC.	BLOOD FLOW, C.C. PER MIN.	PULSE RATE, PER MIN.	TIME INTERVAL FEEDING TO INJECTION, MIN.	CIRCULATION TIME, SEC.	BLOOD FLOW, C.C. PER MIN.	PULSE RATE, PER MIN.	TIME INTERVAL, MIN. AFTER FEEDING	CIRCULATION TIME, SEC.	BLOOD FLOW, C.C. PER MIN.	PULSE RATE, PER MIN.
1	16.5	12.0	184	64	108	8.0	123	96	257	10	90	90
2	17.7	18.2	92	60	65	11.5	292	70	---	--	--	--
3	20.0	20.0	123	86	100	14.5	269	125	373	18	190	114

in pulse rate and volume flow and minimal values of circulation time were found to occur more rapidly after the feeding of a milk-egg-glucose meal than after the ingestion of meat and cereal.

Herrick, Essex, Mann, and Baldes have shown that, during digestion, there is the same type of increase of volume flow in the femoral and carotid arteries and in the external jugular veins as there is in the mesenteric arteries. The results of their experiments also led them to conclude that the increased volume flow of blood during digestion is accounted for chiefly by an increase in the velocity of the blood in the entire circulatory system. Our data support the assumption that an increase in the velocity of flow of blood, evidenced by the decrease in the circulation time of the blood between the jugular vein and the femoral artery, is one of the chief factors.

CONCLUSIONS

1. The circulation time of the blood is decreased (12.9 to 45.4 per cent) during digestion, presumably at its maximal point as judged by the highest pulse rate. The type of meal ingested influences the time at which digestion reaches its maximum and at which the circulation time of the blood is at its minimal value.

2. The decrease in the circulation time of the blood during the processes of digestion is coincident with an increase in pulse rate and also with an increase in the volume rate of blood flow per minute in the femoral artery as measured by a modification of the Rein thermostromuhr.

3. These findings support the deductions of other investigators concerning the effects of digestion on volume rate of blood flow, since our experiments have demonstrated that an increase in velocity of the blood in the entire circulatory system is the chief factor which accounts for increased rate of blood flow.

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ELECTROCARDIOGRAPHY IN INFANTS AND SMALL CHILDREN

Suggestions on the Technic*

R. Earle Glendy, M.D., and Margaret M. Glendy, M.D.
Boston, Mass.

THE difficulties of obtaining satisfactory electrocardiographic tracings from infants and small children are well known to those who have attempted this procedure. Several months ago when we began a series of normal control electrocardiograms on newborn infants it became apparent that the percentage of good tracings obtained with adult-sized electrodes was too small to warrant continuing unless the technic could be improved.

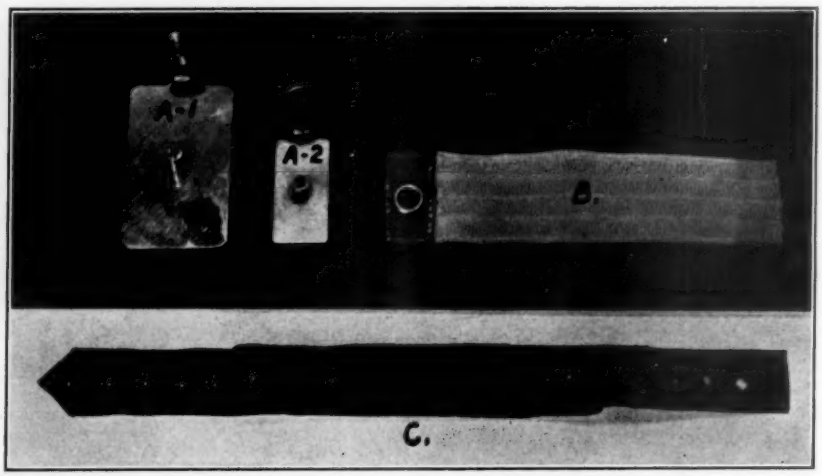

Fig. 1.—*A-1*, electrode for adults; *A-2*, electrode for infants; *B*, retaining strap for extremities; *C*, retaining strap for chest (approximately ⅛ actual size).

The main drawbacks to the use of adults' electrodes were their large size, often resulting in poor electrical contacts when applied to the tiny extremity of an infant, and their weight which resulted in physical restraint and struggling on the part of the infant to free himself. This, in turn, produced the artefacts due to motion so common in infant electrocardiograms.

With these points in mind we have devised a method of obtaining good tracings which, along with the judicious use of a bottle of water and a little patience, has proved satisfactory in every case.

*From the Cardiac Clinic and Laboratory, and the Pediatric Department of the Massachusetts General Hospital.

APPARATUS

The infant-sized electrodes* (Fig. 1, *A-2*) used by us were made of German silver, and are of the same general design as the large electrodes now in common use, but measure only 2 by 4 cm. in area as compared with 3.8 by 6.6 cm. which is the area of the adult-sized electrode (Fig. 1, *A-1*). The central post for attaching the small electrode measures 1.25 cm. in height as compared with 1.65 cm. in the adult's electrode.

A strip of elastic webbing 3.5 cm. wide and 15 cm. long, the end of which was reenforced with leather and a small metal ring, was used to apply the electrodes to each extremity (see Fig. 1, *B*).

From a piece of flat rubber 2 mm. in thickness, a strap (Fig. 1, *C*) 2.5 cm. wide and 50 cm. long was made for applying the chest electrode. On one end of this strap large holes (3.5 mm. in diameter) were made to fit over the base of the central electrode post and on the other end small holes were made (1.5 mm. in diameter) to fit over the tip of the electrode post.

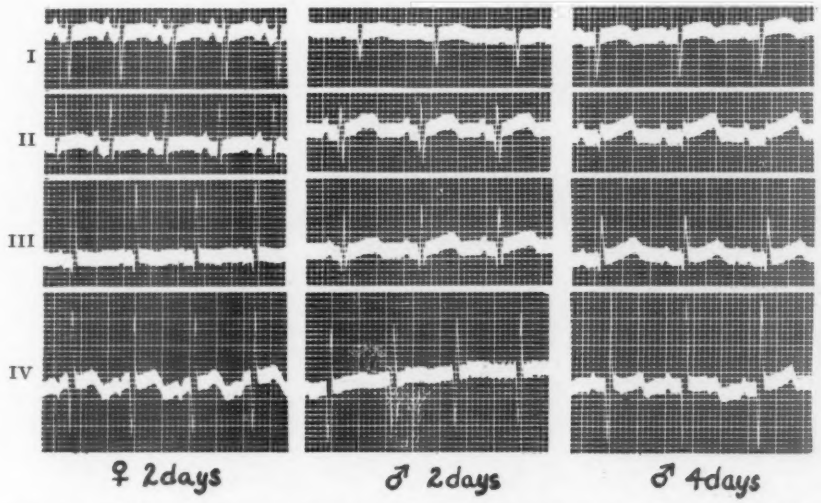

Fig. 2.—Electrocardiograms (Leads I, II, III, and IV) of normal newborn infants.

METHOD

Sanborn redux paste[1] was used as the contact material in applying the electrodes which were placed on the dorsum of the forearms, on the anterior fleshy portion of the left lower leg, and at the cardiac apex to record the chest lead, the leg electrode being left in place as the indifferent electrode. The sites of application, after being cleansed with alcohol, were rubbed gently with a small amount of redux paste and a daub of paste the size of a small pea was smeared on each electrode before it was put in place. The electrodes on the extremities hold firmly in place when the metal ring on one end of the retaining strap is placed over the central post of the electrode at its base and the loose end carried around the extremity and adjusted to the proper snugness by sinking the sharp point of the post into the elastic webbing. Similarly, in applying the electrode to the chest, one of the larger openings at one end of the rubber strap is placed over the base of the central post of the electrode; the strap is then carried around the chest and the electrode made fast by placing one of the many small holes over the tip of the post.

*Made by the Sanborn Company, Cambridge, Mass., under the direction of Mr. J. L. Jenks, Jr.

COMMENT

These modifications in technique are reported because we feel that the good results obtained justify their wider use, and because the cost of the additional necessary equipment is very low. In a report on the "Electrocardiogram in Newborn Infants," which is soon to be published, we will elaborate further on some of the refinements of the technique. Sample tracings are shown in Fig. 2.

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CHARACTERISTIC SERIAL CHANGES IN THE FOURTH LEAD AFTER ACUTE CORONARY THROMBOSIS*

MARCUS A. FEINSTEIN, M.D., AND ABRAHAM LIEBERSON, M.D.
NEW YORK, N. Y.

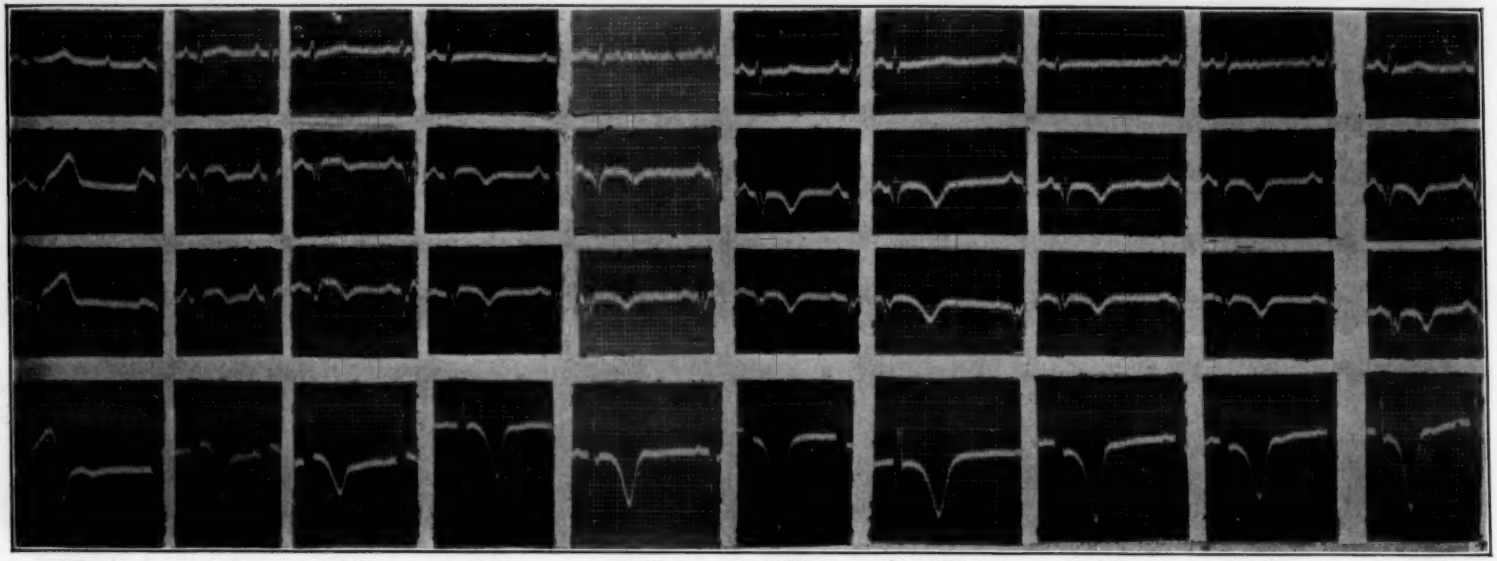
THE electrocardiographic changes in the conventional leads following acute coronary occlusion have been studied in detail since the original descriptions by Smith,[1] Herrick,[2] Pardee,[3] and others. It has been stressed that these findings, such as elevated RS-T segment, deeply inverted coved T-waves, or abnormally deep Q-waves, are not constant—that they may change from day to day during the early period (first few weeks or months) of an acute coronary thrombosis.[4, 5] These serial electrocardiographic changes indicate a recent injury to the heart and help distinguish it from an old thrombosis.

With Wolferth and Wood's clinical introduction of chest leads to the study of coronary thrombosis[6a, 6b] (after the experimental work of Wilson[7]), the accuracy of the electrocardiographic diagnosis of coronary occlusion was still further increased. These workers and many others[8, 9, 10, 11, 12, 13] found Lead IV definitely helpful in indicating the presence of acute thrombosis in a certain number of cases in which the conventional leads were normal, or not characteristic of this condition.

As in the conventional leads, the significant findings in the chest lead following acute thrombosis undergo serial changes from day to day. Tracings showing these progressive changes have been published in several reports,[11, 13, 14, 15] but the subject deserves more detailed and specific study. Familiarity with the whole sequence of typical changes occurring serially in Lead IV after acute coronary thrombosis enables one to detect this condition more readily in any single four-lead electrocardiogram examined. It also helps to time the occurrence of the thrombosis, and distinguish an anginal attack from a true thrombosis. These aspects will be discussed later.

The present study was made on twelve consecutive patients, eleven males and one female, diagnosed acute coronary thrombosis in the medical wards of Beth Israel Hospital. (There were three more cases which were not used because death supervened before serial tracings could be taken.) None of the patients had received digitalis for weeks prior to admission; no digitalis was administered during their hospital stay. The electrocardiograms were taken at the bedside several times during the first week, then once or twice a week for the next four to five weeks, the period of observation averaging six weeks. A follow-up

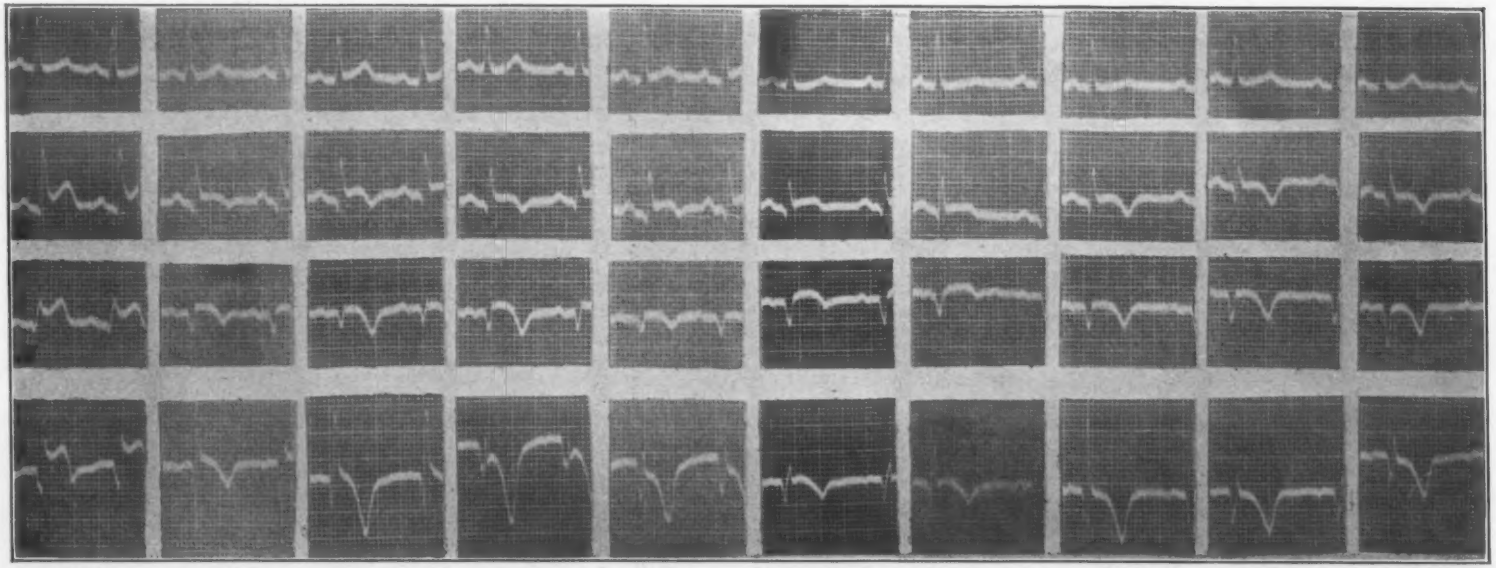
*From the Medical Service of the Beth Israel Hospital.



4/3/36	4/6	4/8	4/11	4/15	4/21	4/28	5/5	5/12	5/28
4 hours	3 days	5 days	8 days	12 days	18 days	25 days	32 days	39 days	55 days

Fig. 1.—Posterior infarction. M. M., No. 81826, male, aged forty-five years. The patient had several attacks of anginal pain for three weeks prior to admission. An anginal attack of unusual severity, not relieved by nitroglycerine or morphine, one hour before admission brought him into the hospital. The first electrocardiogram (April 3, 1936) taken four hours after the attack shows a markedly elevated RS-T segment in Lead IV. The T-wave is negative and already sharply pointed. Note the general similarity in contour of Leads IV, III, and II, and the dissimilarity to Lead I. The fourth lead goes through a period when it appears almost normal (April 8, 1936) except for the raised RS-T segment—a finding much more significant than a similar depression in this lead. The T-wave later (April 11, April 15) becomes suspiciously asymmetrical (cove-planed) in shape; it is already disproportionately large in relationship to the relatively small QRS. The deeply inverted T-waves of April 21 and May 5 are very suggestive of an acute process in the myocardium. In the conventional leads the changes are typical of the Q_3T_3 type (posterior infarction).

The patient was discharged on May 17, 1936, and readmitted May 27, 1936, because of recurrence of precordial pain and dyspnea. Physical examination revealed no new abnormal findings. The electrocardiogram taken the next day (May 28) shows only the slight serial change predictable from the previous infarction. This lack of electrocardiographic evidence of a new coronary closure in the conventional and the fourth leads helped the clinicians decide that the most recent attack of precordial pain was probably anginal in nature and not due to a new infarction.



8/25/36	8/26	8/27	8/28	8/29	9/1	9/3	9/10	9/16	9/23
8 hours	1 day	2 days	3 days	4 days	6 days	8 days	15 days	21 days	28 days

Fig. 2.—Posterior infarction. W. F., No. 85986, male, aged fifty-six years. The initial electrocardiogram (August 25) taken eight hours after the patient's first attack of substernal pain and oppression shows a markedly elevated RS-T segment in Leads II, III, and IV with normal appearing Lead I. On the next day the RS-T elevation is already much less marked, and the T-wave is becoming inverted. This applies to Leads II and III as well as to Lead IV. In the conventional leads a typical Q_3T_3 picture is developing. T_4 is now becoming more and more inverted and abnormally deep in relationship to the small, slurred QRS. This deeply inverted T_4 in the presence of a small QRS is extremely suspicious of posterior infarction, especially when the T-wave is asymmetrical and cove-planed, as in this case. There is not much change in Lead IV after Sept. 16, 1936, and it is likely that the small, slurred QRS and relatively deep T will persist for a while. Note the marked similarity in appearance throughout of Leads II, III, and IV in this case of posterior infarction.

electrocardiogram several months later was obtained in four cases. In the chest lead the anterior electrode (a German silver wire closely wound as a watch spring, 15 mm. in diameter) in every instance was placed in the fourth interspace 6 cm. to the left of the midline, and led to the RA terminal of the string galvanometer. The indifferent electrode was attached to the left leg and the LL terminal. The chest electrocardiogram was taken as Lead II, the resistances being kept below 2,500 ohms by light rubbing of the skin with a toothbrush and salt paste.

When the serial tracings obtained from these twelve patients with acute coronary thrombosis were reviewed, several striking features presented themselves. There was an unusual similarity in the tracings of a good many of the cases, both in the changes and in the speed of progression of the changes. The tracings of several patients were almost exact mirror images of some others (if the isoelectric line were considered the mirror). In short, the electrocardiograms permitted an easy and satisfactory grouping of the serial changes in Lead IV following acute coronary thrombosis into three types.

There is one which we shall call for convenience' sake the deeply negative T_4 (or "posterior") type in which the earliest change (the first day or so after infarction) is marked elevation of the RS-T segment (Figs. 1 and 2). Within the next few days the RS-T elevation becomes less marked and rapidly tends to approach the isoelectric line. Concomitantly with this is a sharp inversion of the T-wave. Often Q_4 becomes increasingly deep and R_4 decreases in size. Within the next few weeks large inverted T-waves are seen from 10 to 25 mm. in depth; they are often cove-planed in this period and of the "coronary" type.[3b] During the next few weeks the T-wave tends to become smaller and more normal appearing. After about two months there is not much in Lead IV indicative of the infarction except perhaps a very deep Q_4 with an abnormally small R_4, or a deeply inverted T_4. This type, with original elevation of RS-T_4 and later negative T_4, is associated with similar RS-T elevations and inversion of the T-waves in Leads II and III. Barnes and Whitten have shown that this "T_3 type" of electrocardiogram indicates infarction of the posterior basal portion of the left ventricle or of the interventricular septum.[16, 17a] The progressive changes in Lead IV outlined above then are to be ascribed to posterior infarction, justifying the name "posterior type of serial change."

The progressive changes in Lead IV of the second group (Figs. 3 and 4), the positive T_4 (or "anterior") type, have characteristics almost exactly opposite to the first. The earliest changes are marked depression of the RS-T segment with a T-wave which very soon becomes positive. As the T-wave grows taller and more positive the RS-T de-

pression becomes less noticeable. Concomitantly there is almost always either a complete loss of the Q_4 deflection, or at least a marked diminution in its size. For the next few weeks the T-wave is likely to be

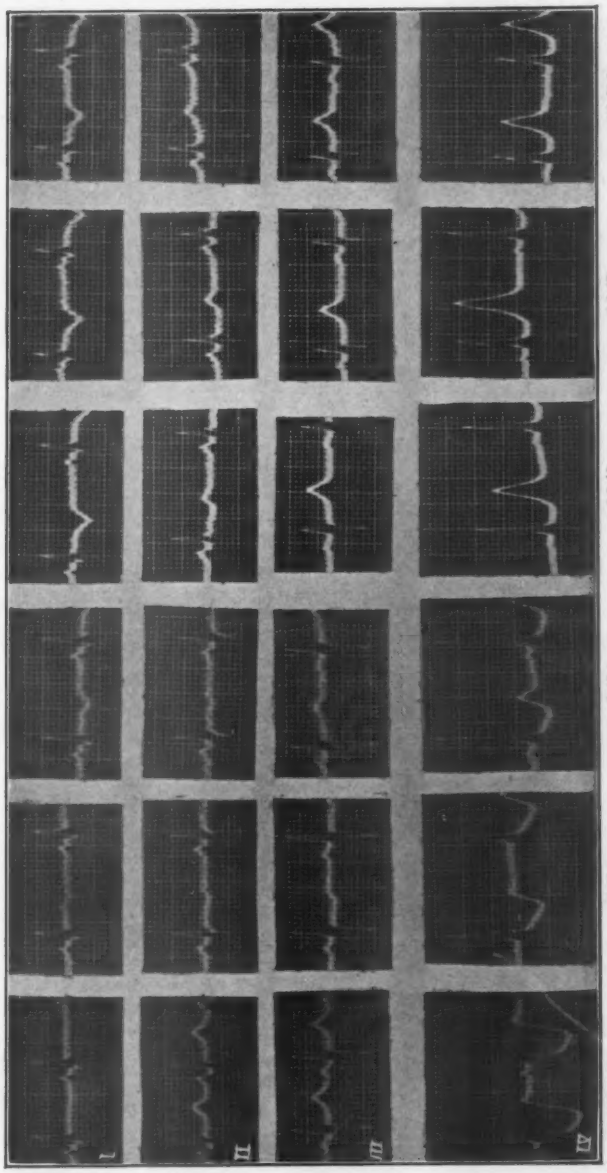


Fig. 3.—Anterior infarction. E. B., No. 86585, male, aged sixty-three years. The first tracing (September 16) was taken three days after a single attack of persistent, dull, substernal burning. While the conventional leads show only a flat T-wave in Lead I with a suggestion of a Q_1 wave, the RS-T segment in Lead IV is strikingly depressed. As this RS-T depression becomes less prominent, the T-wave becomes constantly more positive. Q_4 is absent throughout. The upright T_4 waves are unusually tall (even higher than the QRS on October 5), and indicate the presence of an active cardiac process. The tall T-wave becomes smaller in time. The final (permanent) picture is apt to be an absent Q_4 wave and positive T_4 wave. The conventional leads in this case also show serial changes (inversion of T_1); these changes at first are not as marked in Lead I as in Lead IV and are not as characteristic of acute coronary thrombosis. In Lead IV the serial changes fit nicely into the "anterior infarct" pattern from the start.

unusually tall, and although positive it has the same coved appearance which characterizes the inverted coronary T-wave of Pardee, an observation recently stressed by Wolferth and Wood.[15, 6c] The T-wave later becomes smaller. The changes in Lead IV in this group of cases tend to be more permanent—so that for months and even years many

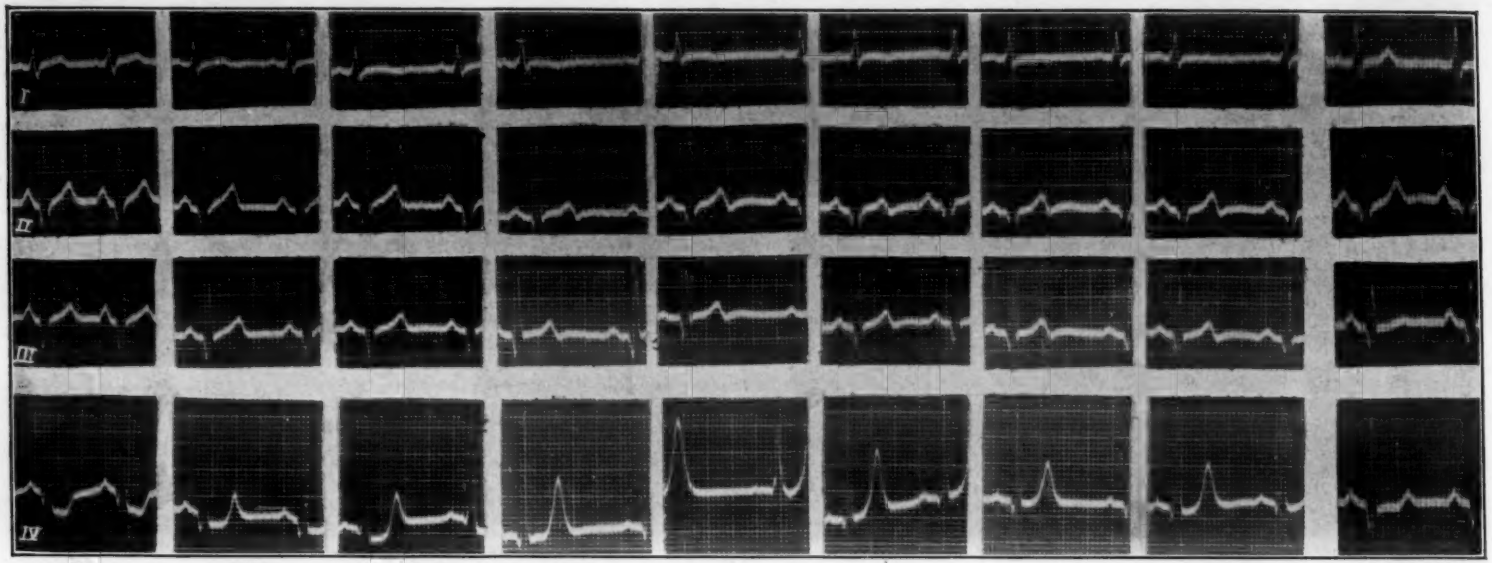


Fig. 4.—Anterior infarction. S. B., No. 82307, male, aged forty-eight years. The patient had several attacks of epigastric pain related to exertion for one month before admission. An unusually severe seizure with radiation of the pain to the interscapular region occurred five days before, and to a lesser degree the day of, admission. The first electrocardiogram taken five days after the severe attack is practically normal in the conventional leads (except for deep Q_3), but shows a marked depression of the RS-T interval in Lead IV. The T-wave cannot be made out clearly. The next electrocardiogram shows RS-T_4 less depressed but T_4 is upright and pointed. As the RS-T segment comes up to the normal level the T-wave becomes taller and more positive. Note that Q_4 is practically absent in all of these tracings, and that on May 5 the high upright T-wave is taller than the slurred QRS. The very tall positive T-waves have the same characteristics as the deeply coved, inverted, Pardee T-waves in the conventional leads. They correspond in this case to the clinically active phase of the infarction (as determined by physical findings, white blood cell count, sedimentation rate, and blood pressure). The tall T-wave soon becomes smaller and less characteristic so that the final picture (taken six months after the infarction, i.e., October 21) is that of a small Q_4 with a normally shaped but upright T_4. It is to be stressed in this case that Lead I shows only minimal serial changes characteristic of anterior infarction, while Lead IV shows grosser and more characteristic serial changes.

cases show the typical picture of infarction of this type—an absent Q_4-wave and positive T_4. The changes in Lead IV described for this group are often associated with RS-T elevation and T inversion in Lead I. This T_1 change, when characteristic, has been found to indicate infarction of the anterior apical portion of the left ventricle or the interventricular septum.[16, 17a, d] The serial changes in Lead IV which have been described in this paragraph as of the "anterior" type are due then to anterior apical infarction.

Of our twelve cases, four showed typical "posterior" type, and four "anterior" type of serial change. Those remaining form a third group of cases (the "indeterminate" type) in which the serial changes in the fourth lead are not characteristic or striking enough to permit easy classification as either one of the two main types outlined above. The cause for this lack of conformance to a definite "anterior" or "posterior" type, such as the presence of multiple infarcts, or the additive effects of old and recent infarction, is discussed later. In these patients the serial changes in the conventional leads are also not striking or characteristic of coronary infarction. In any case, however, the serial changes in this "indeterminate" type, although not fitting into the two main, typical electrocardiographic patterns described above, are marked enough to indicate clearly that an active process is present in the heart. By correlation with the clinical findings we are relatively certain that these changes are due to coronary infarction.

COMMENT

Since all the patients here reported recovered from their cardiac attack, it is not possible to state with accuracy just what pathological process occurred in each case to give the electrocardiographic changes recorded. Our experience with the autopsy findings in cases of coronary thrombosis coincides, however, in the main with those of Parkinson and Bedford, Barnes and Whitten, and Wolferth, who find that a typical Q_3T_3 type of electrocardiogram such as is shown in Figs. 1 and 2 is practically pathognomonic of an infarction in the posterior basal portion of the left ventricle or interventricular septum. Although lacking absolute proof, we are relatively certain that the serial changes shown in these figures are due to posterior infarction. The same considerations hold true for the QRS, RS-T, and T changes in the first lead in Figs. 3 and 4, which indicate an anterior infarction. It is of interest to note how reciprocal the registrations of anterior and posterior infarcts are in the chest lead. Fig. 1 (posterior infarct) is almost exactly the reciprocal to Fig. 3 (anterior infarct). This distinction is fundamental.

It has been stated by Barnes and Whitten, Wolferth and Wood, Wilson, and others that the fourth lead does not register posterior

infarction as well as it does anterior. We believe this view is largely due to the fact that tracings were not taken early enough after the infarction. Thus in Figs. 1 and 2 the RS-T segment deviation is even more marked in Lead IV than in any other lead, and compares with the deviation shown by the anterior infarct in Figs. 3 and 4. A study of Lead IV in Figs. 1 and 2 shows that the marked RS-T elevation after posterior infarction usually lasts only a few days. The later changes are largely those of increasing depth of the inverted T-wave. During this interval of several days between the appearance of the markedly elevated RS-T segment and the markedly inverted T_4 the fourth lead may look fairly normal (Figs. 1 and 2). The lack of early and frequent tracings may then be the reason for the alleged failure of Lead IV to register posterior infarction. Several days later Lead IV shows such marked serial changes (in the increasingly deep T-wave) that the diagnosis becomes much more apparent. This indicates the necessity of obtaining early and frequent electrocardiograms on patients with possible coronary infarction. It is advisable to take the first tracing as soon after the attack as possible; then daily for the first week; then biweekly for the first month or so if there is any doubt as to the clinical or electrocardiographic diagnosis, so that a final evaluation on sufficient grounds can be made.

The fact that the T-wave is normally inverted in Lead IV and that deep negative T-waves, as large as 15 mm., have been reported in normal individuals[14] makes it more difficult to recognize posterior than anterior infarction in this lead after the first few days of marked RS-T deviation are over. Of great help at this time is a *correlative* study of the QRS_4 and T_4 complexes. In a normal individual, when T_4 is deep, QRS_4 is also large (25 to 40 mm.). In posterior infarction, on the other hand, a deep T_4 (10 to 20 mm.) is often associated with a relatively low QRS (Figs. 1 and 2). In fact, QRS is sometimes smaller even than T_4, and is often slurred.

It is to be noted that the serial changes in Lead IV after coronary thrombosis (no matter which type) can be conveniently grouped as early, midperiod, or late, depending upon how soon after the infarction these changes are likely to appear. We can classify the RS-T deviations and the changes in the initial ventricular complex (absence of Q_4, or absence of R_4) as early, making their appearance the first few days. The tall, sharply peaked T-waves are generally characteristic of the midperiod (first to third week); while the late changes seen even months after the infarction are almost exclusively in the ventricular complex—in anterior infarction it is the small or absent Q_4 and positive T_4; in posterior infarction it is the very deep Q_4, or the negative T_4 which is disproportionately deep in comparison with the small QRS.

Both the T and QRS changes following coronary thrombosis may be transient. Of these the T changes are often the only ones seen in mild cases, and are more likely to be ephemeral; while the QRS changes are usually more permanent.

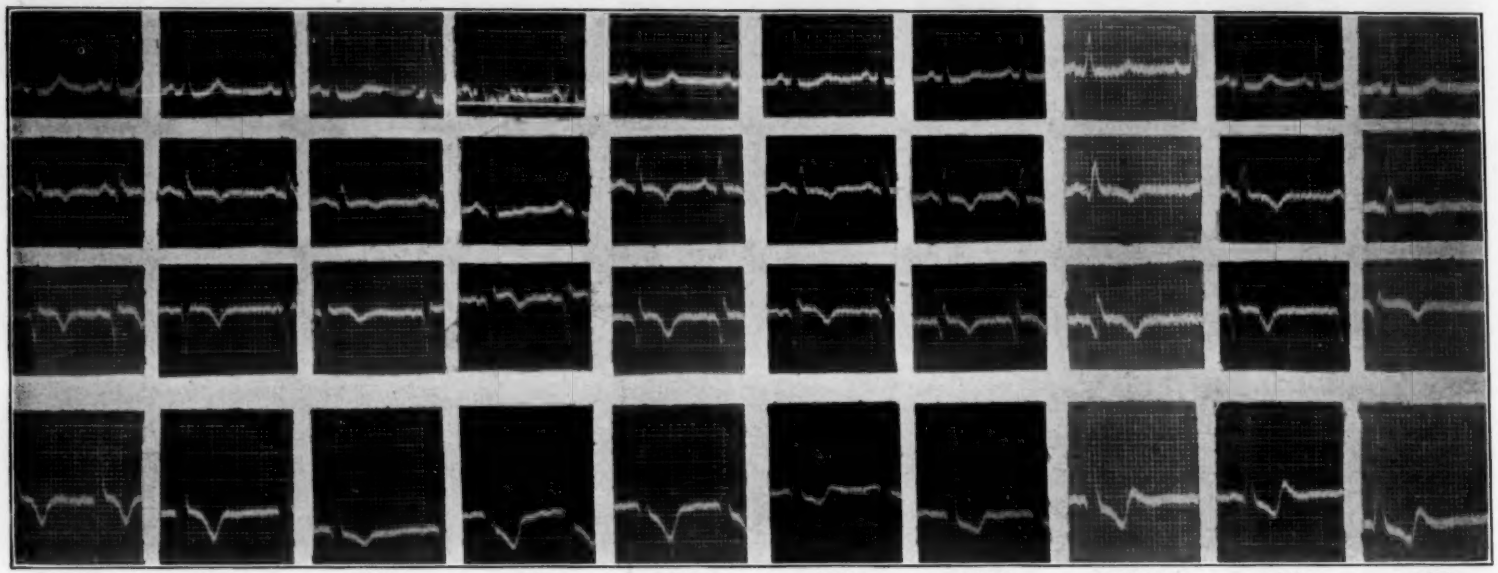
The large positive or negative T_4 waves usually last only a few weeks and appear to be clinically associated with activity of the cardiac process.[15] The treatment that a patient with coronary thrombosis receives is, of course, determined largely by his clinical course; still it is probably wise to consider the process an active one while the T_4 waves are changing rapidly, and to keep the patient at rest.

Aside from the fact that, in general, posterior infarction is known to have a better prognosis than anterior infarction, it appears that those cases which show the characteristic, striking, rapidly changing electrocardiogram in Lead IV (and the conventional leads) fare better clinically than those showing less marked, slower, and less typical electrocardiographic changes. This is probably based on the fact that extensive single infarcts or multiple infarcts involving both the anterior and posterior walls of the left ventricle give electrocardiographic changes which tend to be reciprocal, and balance each other. There are cases (as in Fig. 4) in which the serial changes in the conventional leads are not marked and do not fit easily into a characteristic pattern, but in which the Lead IV changes are prominent and typical. The conformity to type in these cases indicated a favorable prognosis, which the clinical course amply confirmed.

It should be stressed in closing that a familiarity with the serial changes in the fourth as well as in the conventional leads is often of use in confirming a diagnosis of infarction suggested by a single electrocardiogram. In some cases, particularly in anterior infarction, the conventional leads at first were within normal limits, while Lead IV was already definitely suggestive of anterior infarction (Fig. 4). Furthermore, the serial changes in the conventional leads were minimal, while in the fourth lead they were marked and fitted into a characteristic pattern of anterior infarction. In some other cases, as in Figs. 5 and 6, the progressive changes are only slight in the conventional leads and are not as confirmatory of the clinical impression of coronary thrombosis as is Lead IV, where the changes fit into a more diagnostically typical pattern. These considerations form the basis for the use of serial four-lead electrocardiographic studies in the confirmation of the clinical diagnosis of coronary occlusion.

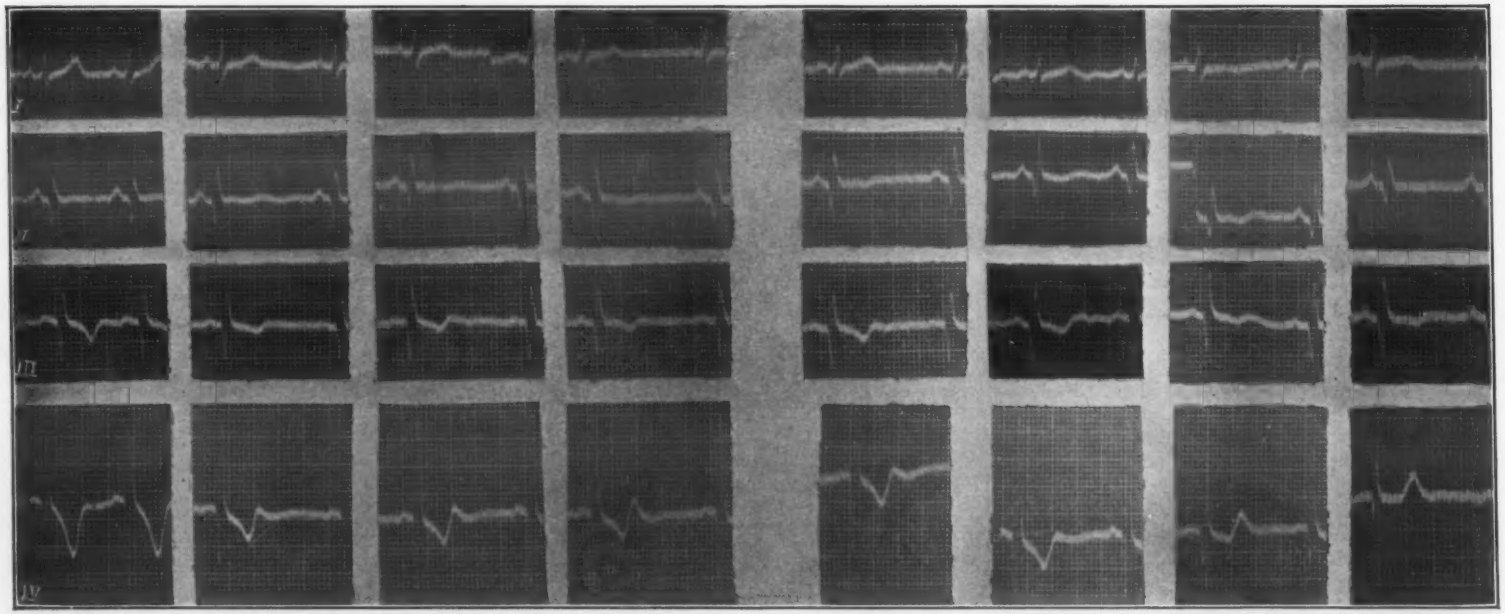
SUMMARY AND CONCLUSIONS

1. Frequent serial four-lead electrocardiograms were obtained on twelve patients with the clinical diagnosis of acute coronary thrombosis. The serial changes in the precordial lead permitted ready group-



12/12/35	12/15	12/16	12/19	12/23	12/27	12/30	1/6/36	1/13	1/21
6 days	9 days	10 days	13 days	17 days	21 days	24 days	31 days	38 days	46 days

Fig. 5.—Indeterminate type. B. K., No. 78904, male, aged forty-nine years. The patient had a two-year history of precordial pain and dyspnea on exertion. Four days prior to admission he experienced severe pain in the precordium radiating to the left shoulder. The first electrocardiogram taken six days after his attack is of the Q_3T_3 type. The RS-T segment in Lead IV is slightly elevated (which is significant). The changes for the next three days (December 15) are the usual predictable serial changes after posterior infarction. On December 16, however, Lead IV shows a sudden turn. Overnight the Q_4 becomes unusually small and remains so. After this the Lead IV serial changes no longer follow the typical pattern of posterior infarction as in Figs. 1 and 2, but begin to show T_4 waves that are biphasic, and finally more positive than negative. On the very day that Q_4 disappeared (December 16) the patient had a recurrence of severe substernal pain, fall in blood pressure, and collapse. Clinically a new coronary closure was postulated. The sudden turn in serial changes on December 16 from the "posterior" to the "anterior" infarct type helped substantiate this conclusion.



10/23/34	7/8/36	7/18	7/27	8/3	8/10	8/20	8/23
4 days	1 day	9 days	20 days	27 days	34 days	44 days	47 days
(first infarct)	(second infarct)						

Fig. 6.—Indeterminate type. M. G., No. 68062, male, aged thirty-eight years. Patient was first admitted Oct. 21, 1934, with precordial pain radiating to the left shoulder for two days. The first electrocardiogram taken shows the typical Q_3T_3 type of change found in posterior infarction. He was readmitted June 14, 1935, with severe precordial pains lasting twelve hours. There was no clinical evidence of a new closure. The serial four-lead electrocardiograms showed no progressive changes and were typical of the posterior infarct type. He was readmitted July 8, 1936, with an attack of precordial pain lasting three hours. He showed clinical evidence of a new closure (fever and fall in blood pressure) and the electrocardiograms (July 8 to Aug. 23, 1936) show serial changes. In the conventional leads they are not prominent, but in Lead IV the inverted T-wave distinctly changes to a diphasic T, which finally (August 23) is entirely upright. Notice that with the second infarction (from the second to the eighth tracing of this figure) the patient shows an "indeterminate type of serial change" in Lead IV, while the first infarction was typically of the "posterior" T_3 type. This often occurs with successive infarctions and was shown by two other cases of the series studied.

ing into three types, the "anterior infarct" type (4 cases), the "posterior infarct" type (4 cases), and the "indeterminate" type (4 cases).

2. Anterior infarction causes serial changes in the chest lead almost exactly opposite to those produced by posterior infarction. In anterior infarction the RS-T segment is at first depressed. As this returns to normal the Q-wave becomes smaller and the T-wave more upright. Soon the classical picture of anterior infarction is shown; absent Q_4, and upright, coved T-wave. Posterior infarction shows at first a markedly elevated RS-T segment in Lead IV. As this returns to normal, Q_4 becomes large, and T_4 is unusually deeply inverted.

3. As in the conventional leads, the RS-T segment changes are likely to be the earliest ones; the markedly coved, sharply peaked or tall T-waves are more characteristic of the midperiod (the first 3 to 4 weeks). The changes which characterize the late stage of coronary thrombosis and which appear to be permanent in a good many cases are the abnormal form of the QRS and the direction of the T-wave. The change in Q_4 (either very deep in posterior infarct or absent in anterior infarct) is often among the first to appear and the last to disappear. Three or four months after the coronary infarction there is little serial change in Lead IV.

4. If electrocardiograms are taken early enough, the presence of a posterior infarct is registered as surely in the fourth lead as an anterior.

5. One should view with suspicion a precordial electrocardiogram which corresponds to any of the tracings published here, for they represent the many changes possible after coronary thrombosis. Particular emphasis is laid on any tracing showing an elevated RS-T segment or a disproportionately deep negative T_4 wave (often seen in posterior infarction).

6. Occasionally a patient will not demonstrate a characteristic pattern of serial changes in the conventional leads and will do so in the chest lead. The fact that the fourth lead serial changes fit into a definite pattern not only helps substantiate the diagnosis of coronary infarction but often permits localization of the infarct.

7. A knowledge of the expected serial changes in the four-lead electrocardiogram is useful in making the differential diagnosis between a second infarction and a simple anginal attack after the original infarction. In the latter there will be no interruption in the sequence of the serial changes due to the original infarction. If a new occlusion occurred, however, the sequence will be interrupted by new findings prominent in all leads, especially the fourth.

8. Cases of coronary thrombosis which give electrocardiographic changes fitting easily into the classical types described above seem to

have better prognoses than the indeterminate type with small, slowly developing, atypical changes. This may be because the infarction is single and not large.

We are extremely indebted to Dr. I. W. Held and Dr. A. A. Epstein on whose medical services these patients were studied, and to Dr. H. Vesell for the cordial cooperation of the electrocardiographic department in this work.

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THE DURATION OF SYSTOLE IN HYPOCALCEMIA*

PAUL S. BARKER, M.D., FRANKLIN D. JOHNSTON, M.D., AND
FRANK N. WILSON, M.D.
ANN ARBOR, MICH.

THE purpose of this paper is to report observations on the duration of "electrical systole" as measured by the Q-T interval of the electrocardiogram, and of "mechanical systole" as measured in records of the heart sounds in the presence of abnormally low blood serum calcium content. It has previously been reported that the Q-T interval of the electrocardiogram is prolonged when the serum calcium is low.

In 1922 Carter and Andrus[1] described prolonged Q-T intervals in six patients with infantile tetany and in three patients with adult tetany, all with low serum calcium values. One of the adult patients had been taking large amounts of sodium bicarbonate, another had pyloric obstruction, while the third had tetany of undetermined origin. In all instances the Q-T interval became shorter as the serum calcium rose in response to treatment.

In 1929 White and Mudd[2] reported prolonged Q-T intervals in two patients with tetany and low serum calcium, and a shortened Q-T interval in one patient with elevated serum calcium. The Q-T intervals returned to normal as the serum calcium values were restored to normal. One other case had normal Q-T intervals, both when the serum calcium was elevated and when it was normal. In one out of five patients with uremia the Q-T interval was prolonged. Systole was not prolonged in patients with hypertension.

In 1932 Spalding's observations were reported by Ballin.[3] He observed that in tetany following thyroidectomy the Q-T interval was prolonged, but that it returned to normal after successful parathyroid transplant. Furthermore, in hyperparathyroidism the Q-T interval was shortened, but returned to normal following parathyroidectomy.

In 1936 Kellog and Kerr[4] reported two patients with hyperparathyroidism and hypercalcemia in which the Q-T intervals were shortened. After operation the serum calcium dropped to normal and the Q-T intervals rose to normal. The shortening of the Q-T intervals was not considered to be sufficiently pronounced to be of value in the clinical diagnosis of hyperparathyroidism.

It has long been known[2, 5-14] that the duration of ventricular systole is related to the heart rate. A number of formulas have been devised to express this relationship. One of the most satisfactory of these

*From the Department of Internal Medicine, University of Michigan Medical School, and the University Hospital.

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formulae is Bazett's,[7] systole = K $\sqrt{\text{cycle}}$. In normal men K was found to vary between 0.342 and 0.392, with an average value of 0.368. In normal women K varied between 0.36 and 0.44, with an average value of 0.399. In our observations we have applied Bazett's formula and have used K as an expression of the duration of systole, thus taking into account the effects of variations in heart rate.

We have recently observed nine patients with abnormally low serum calcium values and abnormally prolonged ventricular systole as measured from the beginning of the Q-wave to the end of the T-wave of the standard electrocardiogram. The essential data are given in Table I.

TABLE I

THE DURATION OF SYSTOLE AS MEASURED IN ELECTROCARDIOGRAMS AND HEART SOUND RECORDS, EXPRESSED IN SECONDS, AND THE CALCIUM AND INORGANIC PHOSPHORUS VALUES OF THE BLOOD SERUM, EXPRESSED IN MG. PER 100 C.C.

CASE	SEX	DIAGNOSIS	ELECTROCARDIOGRAM				BLOOD		
			DATE	SYSTOLE	CYCLE	K (BAZETT'S FORMULA)	DATE	SERUM CA.	SERUM PHOS.
1	F	Hypoparathyroidism	2/18/35	0.47	0.745	0.545	2/16/35	7.8	6.1
			2/19/35	0.46	0.82	0.508			
				0.32	0.815	0.355*	2/26/35	5.4	6.6
			2/27/35	0.52	0.85	0.565			
			2/28/35	0.50	0.78	0.567			
			2/29/36	0.40	0.94	0.413	2/28/36	9.4	5.2
2	F	Hypoparathyroidism	1/28/36	0.40	0.77	0.456	1/28/36	7.3	6.6
			2/29/36	0.425	0.745	0.493	2/29/36	6.2	7.0
				0.36	0.752	0.415*			
			3/17/36	0.40	0.83	0.440	3/17/36	8.3	5.6
3	F	Hypoparathyroidism	3/28/36	0.48	0.84	0.524	3/27/36	5.1	6.5
			3/31/36	0.52	0.985	0.525			
				0.37	0.98	0.375*			
			4/ 1/36	0.43	0.745	0.499	4/ 1/36	6.9	4.8
			4/ 4/36	0.43	0.80	0.481	4/ 4/36	7.7	
			4/ 9/36	0.44	0.88	0.469	4 /9/36	8.4	4.8
4	M	Chronic nephritis, hypertension, uremia	4/13/36	0.40	0.56	0.535	4/15/36	6.0	12.7
			4/16/36	0.43	0.61	0.551			
				0.266	0.60	0.344*	4/17/36	6.7	12.5
5	M	Subacute nephritis, hypertension, uremia	2/26/36	0.46	0.80	0.514	2/26/36	5.2	9.9
			2/27/36	0.535	0.842	0.583	2/27/36	4.8	10.5
				0.335	0.84	0.366*			
6	M	Urethral stricture, chronic pyelonephritis, uremia	2/14/36	0.52	0.83	0.571			
			2/18/36	0.535	1.03	0.527	2/20/36	6.3	
				0.34	1.025	0.336*	2/26/36	6.5	8.2
7	M	Chronic nephritis, hypertension, uremia	5/26/36	0.36	0.66	0.443	5/26/36	8.5	8.4
8	F	Subacute nephritis, hypertension, uremia	5/ 4/36	0.37	0.62	0.471	5/ 5/36	5.2	13.1
9	F	Chronic nephritis, hypertension, uremia	5/ 6/36	0.38	0.66	0.468			
			5/21/36	0.34	0.61	0.436	5/20/36	7.6	10.0

*Mechanical systole as measured in heart sound records.

Three of these patients were women who had hypoparathyroidism and tetany following subtotal thyroidectomy.* In them the response to treatment could be followed sufficiently closely to demonstrate that as the serum calcium rose to normal the duration of systole became shorter (Fig. 1).

The other six patients had nephritis with renal failure and uremia, accompanied by abnormally low serum calcium values. Their electro-

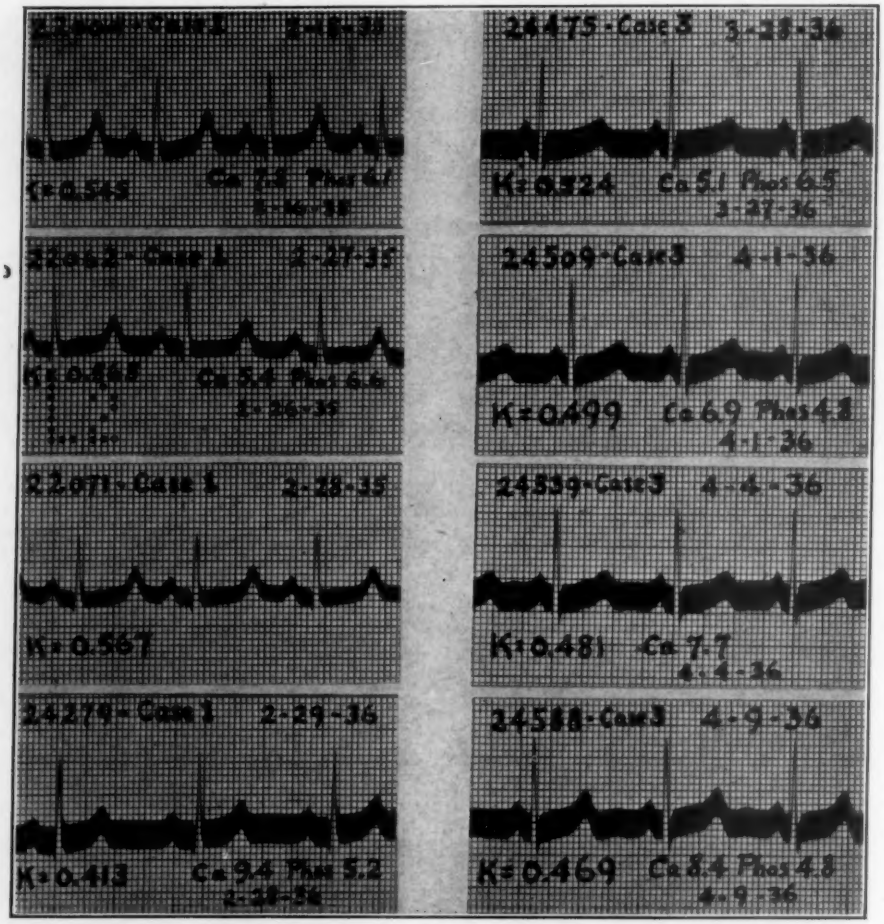

Fig. 1.—Four electrocardiograms, Lead II, of each of two women with hypoparathyroidism following subtotal thyroidectomy. The dates of the curves are given, also the blood serum calcium and phosphorus values in milligrams per 100 c.c., and the dates upon which these determinations were carried out. *K* is the index of the duration of systole as determined from Bazett's formula, systole = $K\sqrt{\text{cycle}}$.

cardiograms showed prolonged Q-T intervals (Fig. 2). They did not live long and it was not possible to observe variations in systole as re-

*Clinical observations and studies of calcium and phosphorus metabolism in two of these patients have been reported by Freyberg, R. H., Grant, R. L., and Robb, M. A. (Hypoparathyroidism, J. A. M. A. 107: 1769, 1936). Their cases 1 and 2 are our cases 2 and 1, respectively.

lated to changes in the serum calcium content. All six of these patients had hypertension. In several of them it was thought, upon admission to the hospital, that hypertensive heart disease was the chief disease from which they were suffering. The electrocardiograms, however, showed such striking prolongation of the Q-T interval as to suggest hypocalcemia. This led to a study of the renal function, and to the discovery of renal failure as the most important condition present. The prolonged Q-T interval may be of diagnostic importance in the recognition of otherwise unsuspected conditions associated with low calcium values.

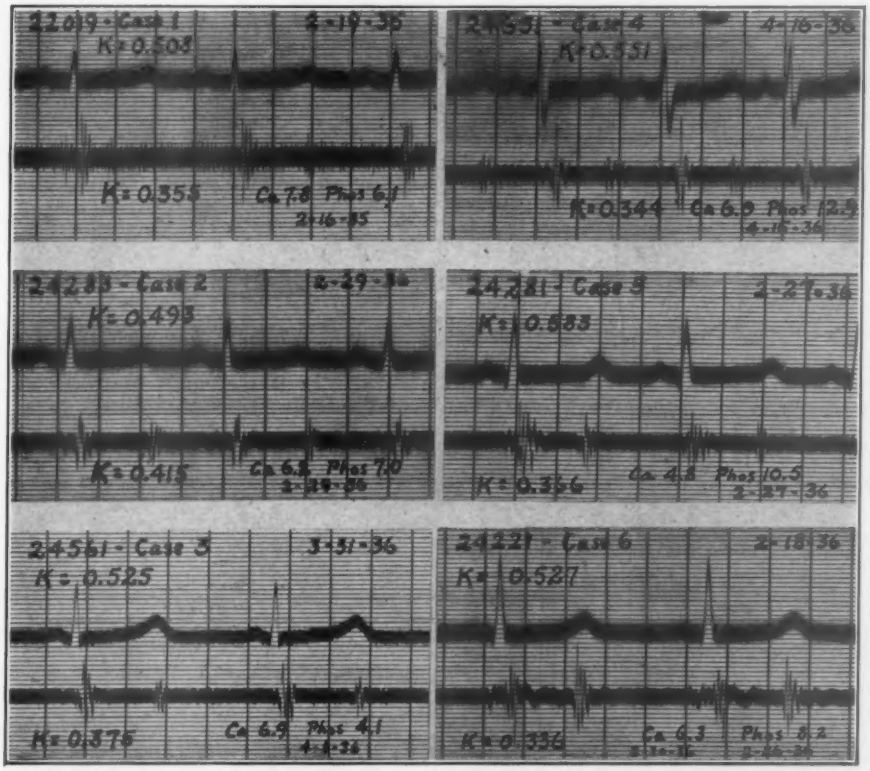

Fig. 2.—Simultaneous electrocardiograms, Lead I, and heart sound records of three patients with hypoparthroidism, first column, and three patients with nephritis and uremia, second column. The dates of the curves and of the determinations of the blood serum calcium and phosphorus determinations are given. *K* is the index of the duration of systole as determined for the electrocardiograms and the sound records from Bazett's formula.

In the three cases of hypoparathyroidism and in three of the cases of nephritis, the heart sounds were recorded simultaneously with the electrocardiogram (Fig. 2). It was found that the duration of systole, as measured from the beginning of the first sound to the beginning of the second sound, was normal. Bartos and Burstein[11] reported in 1924 that in normal men mechanical systole is about 3 to 5 per cent shorter

than electrical systole, as measured respectively in heart sound records and in electrocardiograms. They also found that during altered conditions of the circulation mechanical and electrical systole usually, but by no means always, changed in the same direction, but only rarely to equal degree. In these patients with hypocalcemia, K was from 15 to 37 per cent less for mechanical systole than for electrical systole. In several normal individuals in whom we recorded electrocardiograms and heart sounds simultaneously, K was from 3 to 8 per cent less for mechanical systole than for electrical systole. In one instance it was 3 per cent greater for mechanical than for electrical systole.

SUMMARY

The Q-T interval of the electrocardiogram is abnormally prolonged in the presence of abnormally low blood serum calcium levels. This may be very striking, and may be of diagnostic value in the recognition of otherwise unsuspected conditions associated with hypocalcemia. The duration of mechanical systole, as measured in heart sound records, is not prolonged in hypocalcemia.

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THE POSTURAL EFFECTS ON BLOOD PRESSURE FOLLOWING INTERRUPTION OF THE VASOMOTOR NERVES OF MAN*

GRACE M. ROTH, PH.D.†
ROCHESTER, MINN.

BLOOD pressure is maintained by the minute output from the heart, the volume of blood, the elasticity of the blood vessels, and the peripheral resistance. Under normal conditions the quantity of blood remains the same for fairly long periods of time; elasticity of the blood vessels is a minor factor and is associated with the peripheral resistance. Blood pressure, as a result, is more closely dependent on the energy of the heart and the peripheral resistance. These conditions are controlled by nervous, chemical, and mechanical factors which interact to maintain blood pressure at a constant level. The nervous control, or vasomotor mechanism, includes an efferent portion, associated with the peripheral vascular system, which regulates the size of the peripheral vascular bed. This is under control of a central mechanism. The efferent portion has its effect, for the most part, on the arterial side of the circulation, more precisely on the arterioles rather than on the larger arteries.

The vasomotor nerves to the splanchnic region control the greater portion of the blood vessels of the abdominal viscera. Inasmuch as a large part of the total blood in the body is contained in this region, in animals the general arterial blood pressure is more markedly altered by section of the splanchnic nerves than by section of any other nerves in the body. In man, an upright animal, in the change from the horizontal to the upright position, the splanchnic nerves should, no doubt, play a predominant rôle in the maintenance of blood pressure.

I desired to determine what happens to blood pressure and pulse rate when voluntary change from the recumbent to the upright posture was made by persons whose splanchnic nerves had been interrupted. The following types of men or women were studied: (1) as controls, those whose condition was normal; (2) also as controls, those whose blood pressure and pulse rate were normal before operation but whose vasomotor pathways to the abdominal viscera had been interrupted for postcholecystectomy pain or megacolon; (3) those whose vasomotor pathways to the abdominal viscera had been interrupted because of hypertension. In addition, the response in the vasomotor system following the operations referred to in the foregoing sentences resembles the vaso-

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†Fellow in Physiology, The Mayo Foundation.

motor response of patients who have orthostatic hypotension. For comparison, therefore, it was considered desirable to record the change in blood pressure and pulse rates of patients who had orthostatic hypotension when they voluntarily changed from the recumbent to the upright posture.

The concept underlying the work was accepted as worthy of investigation by the late Dr. G. E. Brown when it was still in the realm of speculation. The investigation was pursued with his cooperation and with that of Doctors Adson, Craig, Mann, Essex and Allen.

METHODS

A standard mercury manometer was used for all determinations of blood pressure. Generally the cuff was placed on the upper part of the right arm of the subject and the calibrated mercury scale stood as high above the floor as the mattress of a bed.

The variations in blood pressure and pulse rate were observed (1) with the subject horizontal, after he had been lying quietly for a half hour, and (2) following his voluntary change to the upright position. This period of rest was particularly necessary if the blood pressure of the patients who had hypertension was to reach a basal level. Observations of blood pressure were made until two consecutive readings of the systolic pressure were within 2 mm. of each other and two consecutive readings of the diastolic pressure were likewise within 2 mm. of each other. The pulse rate was noted simultaneously with the reading of blood pressure. The voluntary change from the horizontal position to the upright one was made with the least possible muscular effort. Observations of blood pressure and pulse rate were noted one and two minutes after the change. The readings made after two minutes were recorded. Since patients with hypertension are most sensitive to psychic stimulation, the upright position was attained by voluntary movement of the patient rather than by means of the tilt table; motion of the tilt table tends to startle patients. Whenever a change in posture is mentioned in this paper, the change is always from the horizontal to the upright position.

The severity of the hypertension was graded by Dr. Wagener,[13] according to the appearance of the retinal arterioles and the presence or absence of retinitis. His classification is as follows: Group I, minimal amount of narrowing or sclerosis; Group II, moderate amount of sclerosis without active spasm; Group III, retinitis with moderate spasm and sclerosis, and Group IV, retinitis with spasm, sclerosis, and choked disks.

Resection of the splanchnic nerves, for lowering the blood pressure of patients with hypertension, was first suggested by Daniélopolu[6] in 1923. In 1924 Pende[7] proposed, before the Congress of Internal Medicine at Milan, surgical treatment of arterial hypertension which consisted of resecting the left splanchnic nerves. Adson,[11] in 1925, performed bilateral lumbar sympathetic ganglionectomy and trunk resection in an attempt to lower the blood pressure. The operation included the second, third, and fourth lumbar ganglions on both sides, but definite drop in blood pressure did not occur. Neither did unilateral cervicothoracic sympathetic ganglionectomy produce an effect on the blood pressure of a patient who had hypertension. Following this, several foreign surgeons[8, 9] performed unilateral splanchnic resection on patients with hypertension and other arterial diseases, with some favorable results.

In 1930, Adson,[3] with the aid of Craig, sectioned the ventral roots of both sides from the sixth thoracic to the second lumbar inclusive. This operation is known as extensive bilateral, ventral rhizotomy. The systolic blood pressure dropped from 200 mm. to 100 mm. of mercury; unfortunately, postoperative hemorrhage developed, and although the clot was removed, partial spastic paraplegia developed and persisted. At this time this procedure was discontinued as an unsatisfactory one.

Craig,[5] in 1932, performed posterior, infradiaphragmatic resection of the splanchnic nerves with removal of the first lumbar ganglion. The operation was applied first to one side and then a similar technic was employed ten days to two weeks later on the other side. For convenience, this operation is designated as posterior, infradiaphragmatic, bilateral resection of the splanchnic nerves and bilateral removal of the first lumbar ganglions.

Since the patient on whom extensive rhizotomy had been performed still maintained a decrease in systolic and diastolic pressure after three years, with results far more striking than those produced by bilateral posterior, infradiaphragmatic resection of the splanchnic nerves and removal of the first lumbar ganglions, Adson[2] returned to extensive, bilateral, ventral rhizotomy in 1933. Whereas, in some of the cases the extensive, bilateral, ventral rhizotomy extended from the fifth thoracic to the second lumbar segments, inclusive, a modified operation was used in other cases so that in some instances the bilateral, ventral rhizotomy included the eleventh thoracic to the second lumbar inclusive, the tenth thoracic to the second lumbar inclusive, the ninth thoracic to the second lumbar inclusive, the eighth thoracic to the second lumbar inclusive, the seventh thoracic to the second lumbar inclusive, and the sixth thoracic to the second lumbar inclusive. In two instances, the ventral nerve roots from the sixth thoracic to the twelfth thoracic, inclusive, were sectioned. In two other instances, the extensive, ventral rhizotomy was performed in two stages, first from the tenth thoracic to the second lumbar, inclusive, and later from the sixth to the ninth thoracic, inclusive.

As the extensive rhizotomy, whether done in one or in two stages, was a formidable procedure, Adson,[3] in 1935, performed extensive resection of splanchnic nerves with partial removal of the celiac ganglion, removal of the first and second lumbar sympathetic ganglions and intervening trunks, and partial resection of the suprarenal gland. This operation was done in two stages, first on one side and, about two weeks later, on the other side.

Following the surgical procedures, readings of blood pressure and of pulse rate were not made until sufficient time had passed to eliminate all aspects of shock and general weakness. The period chosen was twenty-five to twenty-eight days after rhizotomy and the same length of time after the second operation of the two-stage procedure.

The methods used for determining the approach to completeness of the sympathetic denervation were a sweating test[10] performed by the cobaltous chloride and heat method and determination of the cutaneous increase in temperature[12] of the lower extremities. The cutaneous temperature was measured by means of the thermocouple described by Sheard.

MATERIAL

The readings of blood pressure and of pulse rate were determined on 183 subjects before and following voluntary change from the horizontal to the upright position. The subjects were divided into two major groups, depending on whether surgical procedures had or had not been performed.

Group I, or the group composed of subjects who were not operated on, included ninety individuals, and these were divided into two classes, description of which will appear in the respective paragraphs under "Results."

Group II, or the group composed of patients who were operated on, included ninety-three individuals, and these were divided into eight classes, description of which also will appear in the respective paragraphs under "Results."

RESULTS

Group I. Subjects Not Subjected to Operation

Class 1. Normal Subjects.—The individuals of this class consisted of eighty physicians, nurses and other persons; all were in good health as far as could be determined. Their ages ranged from twenty to sixty years, inclusive, with an average age of thirty-four years. Assumption of the upright posture by these persons produced an average increase of 8 mm. in diastolic blood pressure and no increase in the systolic pressure. The cardiac rate increased an average of fourteen beats per minute (Table I).

TABLE I

AVERAGE VALUES OF BLOOD PRESSURE AND PULSE RATE FOR NORMAL INDIVIDUALS

	CASE	AGE (YEARS)	LYING			STANDING		
			BLOOD PRESSURE (MM. HG)		PULSE (BEATS PER MINUTE)	BLOOD PRESSURE (MM. HG)		PULSE (BEATS PER MINUTE)
			SYSTOLIC	DIASTOLIC		SYSTOLIC	DIASTOLIC	
Females	43	30.3	113.8	73.4	77.0	114.9	81.1	90.0
Males	37	37.6	114.5	71.2	75.3	112.6	80.7	91.1
Postural change, females			+1.1	+7.7	+13.0			
Postural change, males			-1.9	+9.5	+15.8			
Age 20 to 30 yr.	35		117.4	71.4	74.1	116.2	82.1	90.1
Age 30 to 40 yr.	24		112.2	72.8	77.0	115.3	82.8	87.7
Age 40 to 50 yr.	13		112.2	73.2	76.9	111.5	76.5	93.8
Age 50 to 60 yr.	8		109.0	74.3	82.2	102.8	77.1	95.3

TABLE II

BLOOD PRESSURE AND PULSE RATE WITH POSTURAL CHANGE IN CASES OF POSTURAL HYPOTENSION

	CASE	AGE (YEARS) AND SEX	LYING			STANDING		
			BLOOD PRESSURE (MM. HG)		PULSE (BEATS PER MINUTE)	BLOOD PRESSURE (MM. HG)		PULSE (BEATS PER MINUTE)
			SYSTOLIC	DIASTOLIC		SYSTOLIC	DIASTOLIC	
	1	44 M	120	92	84	60	44	88
	2	44 M	128	98	76	40		76
	3	64 M	138	90	80	64		88
	4	56 M	130	70	68	40		64
	5	45 M	135	95	75	50		
	6	55 M	130	80	84	85	50	96
	7	55 F	120	70	68	42		100
	8	35 M	128	78	60	88		Syncope
	9	41 F	168	108	84	60	54	100
	10	41 M	100	75	68	45	35	108
Average		48	129.7	85.6	74.7	57.4	45.7	90
Postural change			-72.3	-39.3	+15.3			

Class 2. Patients Who Had Postural Hypotension.—In this class were ten persons, whose ages ranged from thirty-five to sixty-four years inclusive, with an average age of forty-eight years. They are included in the report because abnormal findings associated with function of the vasomotor system were similar to those produced by certain operations on the sympathetic nervous system. The effects on blood pressure and pulse rate of rising from a lying to an upright posture are given in Table II.

Group II. Patients Subjected to Operation

Class 1. Patients Subjected to Various Surgical Procedures Other Than on the Sympathetic Nervous System.—The individuals of this class consisted of thirty-five patients. Their ages ranged from sixteen to

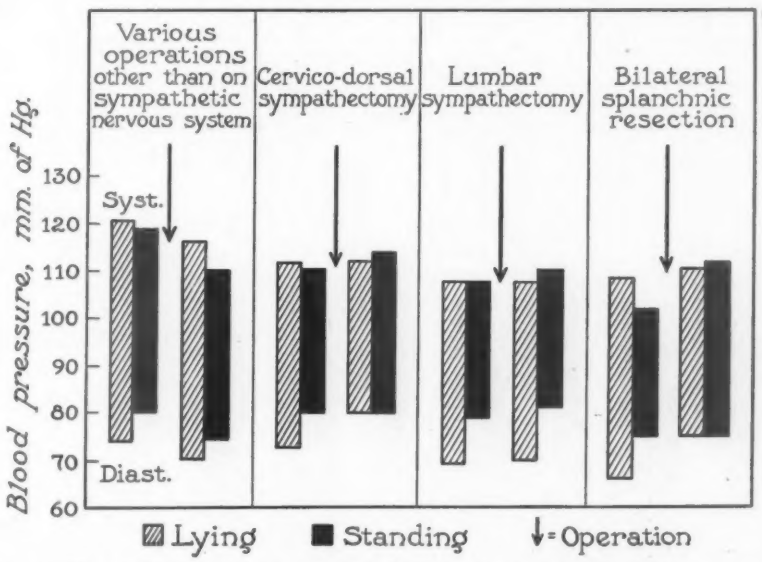

Fig. 1.—The effects of posture and operation on blood pressure. Before operation, the blood pressure of the patients represented was normal. From left to right the columns represent Classes 1, 2, 3 and 5.

seventy years, with an average age of forty-two years. The average blood pressure was 120 mm. of mercury systolic and 75 mm. diastolic. The patients were subjected to cholecystectomy, appendectomy, nephrectomy and laminectomy. The studies were made on this class to determine the effect of operation, if any, on the blood pressure and pulse rate, and the effect on the postural changes in blood pressure. Results are given in Tables III and IV and in Fig. 1.

Class 2. Patients Subjected to Bilateral Cervicothoracic Sympathectomy (Adson-Craig Technique[1]).—In this class were five patients, four of whom had Raynaud's disease and one of whom had essential hyperhidrosis. Their ages ranged from eighteen to thirty-five years, with an average age of twenty-eight years. Their blood pressure was within normal range. Results appear in Tables III and IV and Fig. 1.

TABLE III

THE AVERAGE INCREASE (+) OR DECREASE (-) IN BLOOD PRESSURE AND PULSE RATE AFTER VOLUNTARY CHANGE FROM THE HORIZONTAL TO THE UPRIGHT POSITION

CLASS	SUBCLASS	SUBJECTS	OPERATION	BEFORE OPERATION			AFTER OPERATION		
				CHANGE IN BLOOD PRESSURE (MM. HG)		CHANGE IN PULSE RATE (BEATS PER MIN.)	CHANGE IN BLOOD PRESSURE (MM. HG)		CHANGE IN PULSE RATE (BEATS PER MIN.)
				SYSTOLIC	DIASTOLIC		SYSTOLIC	DIASTOLIC	
1		35	Various major surgical procedures other than on the sympathetic nervous system	- 1.9	+ 5.7	+22.1	- 5.9	+ 2.2	+20.8
2		5	Bilateral cervicothoracic sympathectomy	+ 0.8	+ 6.6	+13.6	+ 0.8	+10.8	+11.0
3		6	Bilateral lumbar sympathectomy	0.0	+ 8.6	+18.7	+ 2.0	+11.7	+24.3
4		1	Bilateral section of intercostal nerves—7th to 11th inclusive	+20.0	0.0	+ 4.0	-20.0	0.0	+ 6.0
5		2	Bilateral section of splanchnic nerves with bilateral removal of the 1st and 2nd lumbar ganglions	- 5.0	+ 2.5	+20.0	+ 2.5	0.0	+47.0
6		6	Posterior infradiaphragmatic bilateral resection of splanchnic nerves and bilateral removal of the 1st lumbar ganglions	-9.0	+ 8.4	+11.8	- 9.1	+ 3.2	+12.3
7	1	1	Bilateral ventral rhizotomy, 11th thoracic—2nd lumbar, inclusive	0.0	+10.0	+22.0	-15.0	- 5.0	0.0
	2	6	Bilateral ventral rhizotomy, 10th thoracic—2nd lumbar, inclusive	- 9.8	+ 3.0	+17.1	-24.0	- 1.6	+16.0
	3	5	Bilateral ventral rhizotomy, 9th thoracic—2nd lumbar, inclusive	-19.0	+ 1.0	+13.6	-19.4	- 5.0	+19.2
	4	1	Bilateral ventral rhizotomy, 8th thoracic—2nd lumbar, inclusive	-34.0	+10.0	+12.0	-40.0	-15.0	+ 8.0
	5	1	Bilateral ventral rhizotomy, 7th thoracic—2nd lumbar, inclusive	+20.0	+10.0	+28.0	-70.0	-40.0	+40.0
	6	2	Bilateral ventral rhizotomy, 6th thoracic—12th thoracic	-16.0	+12.5	+14.0	-12.5	0.0	+24.5
	7	7	Bilateral ventral rhizotomy, 6th thoracic—2nd lumbar, inclusive	-21.4	- 3.9	+18.9	-49.8	-21.9	+29.6
	8	3	Bilateral ventral rhizotomy, 5th thoracic—2nd lumbar, inclusive	-11.0	+ 1.6	+10.0	-28.3	-16.6	+14.7
8		12	Bilateral splanchnic resection, partial resection of the celiac plexus and bilateral partial resection of the suprarenal glands, with bilateral removal of the first and second lumbar ganglions and the intervening trunks	- 0.5	+ 5.3	+12.0	-21.4	-10.5	+32.9

Table IV

The Average Increase (+) or Decrease (-) in Blood Pressure and Pulse Rate as a Result of Operation*

Class	Subclass	Subjects	Operation	Horizontal position change in blood pressure (mm. Hg)		Change in pulse rate (beats per minute)	Upright position change in blood pressure (mm. Hg)		Change in pulse rate (beats per minute)
				Systolic	Diastolic		Systolic	Diastolic	
1		35	Various major surgical procedures other than on the sympathetic nervous system	- 4.5	- 2.9	+ 2.1	- 8.5	- 6.4	+ 1.8
2		5	Bilateral cervicothoracic sympathectomy	+ 0.8	+ 1.2	+ 8.0	+ 0.8	+ 6.4	+ 5.4
3		6	Bilateral lumbar sympathectomy	0.0	+ 1.6	- 1.3	+ 1.8	+ 4.7	+ 4.3
4		1	Bilateral section of intercostal nerves—7th to 11th, inclusive	+30.0	+10.0	+ 6.0	-10.0	+10.0	+ 8.0
5		2	Bilateral section of splanchnic nerves with bilateral removal of 1st and 2nd lumbar ganglions	+ 3.5	+ 2.5	+17.0	+10.0	0.0	+44.0
6		6	Posterior infradiaphragmatic bilateral resection of splanchnic nerves and bilateral removal of the first lumbar ganglions	-14.0	- 3.8	+ 4.5	-14.1	- 8.9	+ 5.0
7	1	1	Bilateral ventral rhizotomy, 11th thoracic—2nd lumbar, inclusive	- 5.0	+10.0	+ 8.0	-20.0	- 5.0	-14.0
	2	6	Bilateral ventral rhizotomy, 10th thoracic—2nd lumbar, inclusive	-19.0	- 5.5	+ 5.1	-32.3	-10.1	+ 4.0
	3	5	Bilateral ventral rhizotomy, 9th thoracic—2nd lumbar, inclusive	-30.0	-17.0	+ 6.4	-30.4	-23.0	+12.0
	4	1	Bilateral ventral rhizotomy, 8th thoracic—2nd lumbar, inclusive	-34.0	-20.0	- 6.0	-40.0	-45.0	-10.0
	5	1	Bilateral ventral rhizotomy, 7th thoracic—2nd lumbar, inclusive	-10.0	-20.0	-12.0	-100.0	-70.0	0.0
	6	2	Bilateral ventral rhizotomy, 6th thoracic—12th thoracic, inclusive	-40.0	-12.5	-15.5	-36.5	-25.0	- 5.0
	7	7	Bilateral ventral rhizotomy, 6th thoracic—2nd lumbar, inclusive	-44.3	-27.2	+ 4.6	-72.6	-45.2	+15.3
	8	3	Bilateral ventral rhizotomy, 5th thoracic—2nd lumbar inclusive	-61.0	-38.4	+ 9.3	-78.3	-56.6	+14.0
8		12	Bilateral splanchnic resection, partial resection of the celiac plexus and bilateral partial resection of the suprarenal glands, with bilateral removal of the first and second lumbar ganglions and the intervening trunks	-42.7	-18.5	+ 1.1	-63.6	-34.3	+21.8

*The purpose of this table is not to be confused with that of Table III. Whereas the primary purpose of Table III is to show the effect of change in posture, the primary purpose of Table IV is to show the effect of operation.

Class 3. Patients Subjected to Bilateral Lumbar Sympathectomy (Adson-Craig Technique[1]*).*—In this class were six patients, one of whom had Raynaud's disease, four of whom had chronic infectious arthritis and one of whom had thromboangiitis obliterans. Their ages ranged from fourteen to forty-three years with an average age of thirty-two years. The blood pressure readings were within normal range. Results appear in Tables III and IV and Fig. 1.

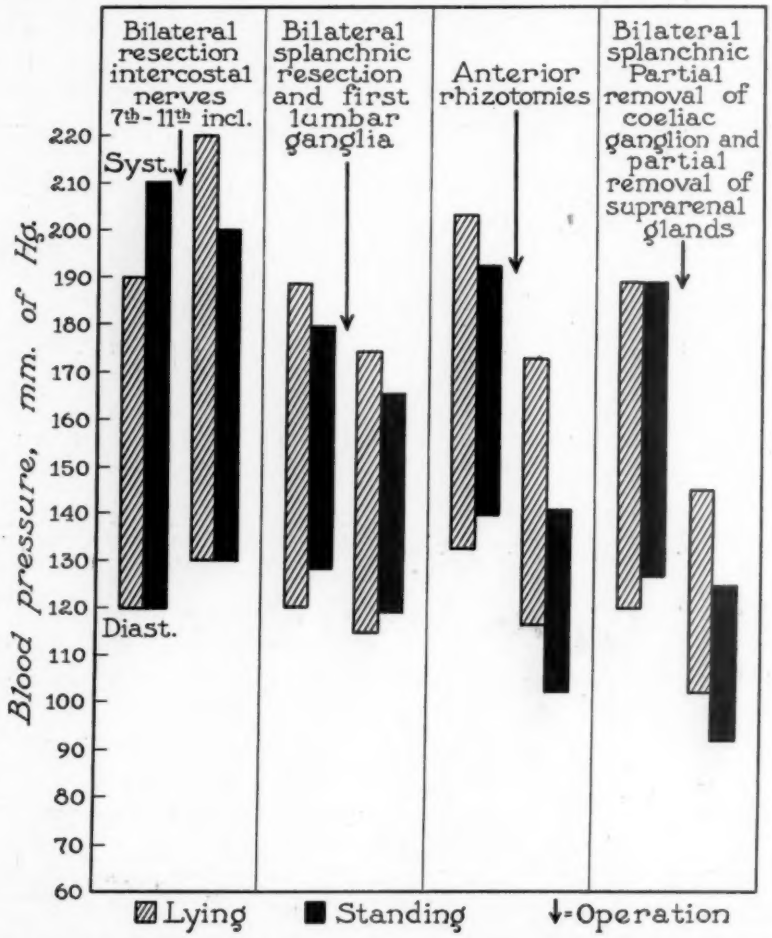

Fig. 2.—The effects of posture and operation on blood pressure. The patients had essential hypertension. From left to right the columns represent Classes 4, 6, 7 and 8.

Class 4. A Patient Subjected to Bilateral Section of Intercostal Nerves From the Seventh to the Eleventh, Inclusive.—This class is represented by only one patient. He was fifty-three years of age and had essential hypertension of a severity which would place his case in Wagener's Group III. This operation was performed because some of the patients with postural hypotension and some of the patients follow-

ing ventral rhizotomy had experienced, when in the upright position, an elevation of blood pressure above the level of syncope, after application of a tight abdominal binder. Therefore, the suggestion was made that relaxation of the intercostal and abdominal muscles would decrease the blood pressure, particularly when the subject was in the upright position. Results are given in Tables III and IV and Fig. 2.

Class 5. Patients Subjected to Bilateral Section of Splanchnic Nerves, With Bilateral Removal of the First and Second Lumbar Ganglions.—This class is represented by two patients, one aged twenty-two years and the other forty-one years, whose blood pressure was normal. Operation was performed for postcholecystectomy pain in one case and for megacolon in the other. Results are given in Tables III and IV and Fig. 1.

Class 6. Patients Subjected to Posterior Infradiaphragmatic Bilateral Resection of Splanchnic Nerves and Bilateral Removal of the First Lumbar Ganglions.—This class is represented by six patients who had essential hypertension. Their ages ranged from twenty-two to forty-six years, with an average age of thirty-seven years. The average systolic blood pressure in the horizontal position before operation was 188.1 mm. The average diastolic blood pressure in the horizontal position before operation was 119.1 mm. Other data are given in Tables III and IV and Fig. 2.

Class 7. Bilateral Ventral Rhizotomy.—This class is represented by twenty-six patients, all of whom had essential hypertension of varying severity. The class is divided into eight subclasses, depending on the extent of the rhizotomy.

Subclass 1. Bilateral ventral rhizotomy from the eleventh thoracic to the second lumbar, inclusive. The operation at this level was performed on one woman, aged twenty-eight years, who had essential hypertension, which by Wagener's classification would be of Group II. The systolic blood pressure in the horizontal position before operation was 185 mm. of mercury and the diastolic blood pressure under the same conditions was 120 mm. The pulse rate, before operation, increased from 88 beats per minute in the horizontal position to 110 beats in the upright position. Other data are given in Tables III and IV and in Figs. 2 and 3.

Subclass 2. Bilateral ventral rhizotomy from the tenth thoracic to the second lumbar, inclusive. Six patients were operated on at this level. The ages ranged from thirty-seven to fifty-one years, with an average age of forty-four years.

All the patients except one had very severe essential hypertension, Group III or IV (Wagener's classification). The hypertension of the exceptional patient was of Group II. Before operation, with the patient in the horizontal position, the average systolic blood pressure was 194.6 mm. Following operation, when the patient was in the horizontal posi-

tion, the average systolic blood pressure was 175.6 mm. The postural change in this group was more than twice as great following operation as before operation. The average diastolic blood pressure before operation was 121.3 mm. Other results are given in Tables III and IV and in Figs. 2 and 3.

Subclass 3. Bilateral ventral rhizotomy from the ninth thoracic to the second lumbar, inclusive. Five patients were operated on. The ages ranged from forty-four to fifty-three years, with an average age of fifty years. They all had essential hypertension (Wagener's Group III). The average systolic blood pressure in the horizontal position before operation was 215 mm. This decreased to 196 mm. when the up-

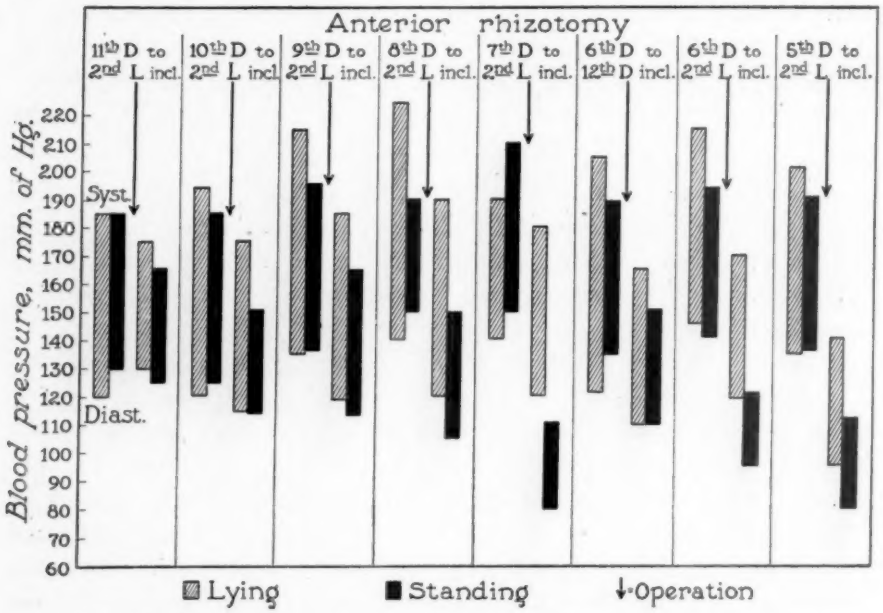

Fig. 3.—The effects of posture and operation on blood pressure. The patients had essential hypertension. The columns represent, in order from left to right, the eight subclasses of Class 7.

right position was assumed. In this group the postural change of the systolic blood pressure before and after operation was the same, even though the actual pressure in both positions was 30 mm. less after operation than before operation. Before operation the average diastolic blood pressure was 136 mm. when the patient was in the horizontal position and remained the same when he assumed the upright position. The average pulse rate before operation, in the horizontal position, was 76.8 beats per minute. Other data are give in Tables III and IV and in Figs. 2 and 3.

Subclass 4. Bilateral ventral rhizotomy from the eighth thoracic to the second lumbar, inclusive. One patient, aged thirty-six years, who

had essential hypertension of Wagener's Group II, underwent rhizotomy at this level. Before operation, with the patient in the horizontal position, the systolic blood pressure was 224 mm. The changes of the systolic pressure resulting from posture were definitely decreased both before and after operation. The diastolic blood pressure in the horizontal position, before operation, was 140 mm. The pulse rate in the horizontal position before operation was 88 beats per minute. Other results are given in Tables III and IV and in Figs. 2 and 3.

Subclass 5. Bilateral ventral rhizotomy from the seventh thoracic to the second lumbar, inclusive. One patient, aged thirty years, who had essential hypertension, Group IV (Wagener's classification), was subjected to this operation. The systolic blood pressure before operation, in the horizontal position, was 190 mm. Following operation, in the change from the horizontal to the upright posture, the systolic blood pressure changed markedly in comparison with the postural change before operation. The diastolic blood pressure in the horizontal position before operation was 140 mm. After operation, in the change from the horizontal to the upright posture, the diastolic pressure decreased to a level of 80 mm. of mercury. This was 50 mm. less than the postural change before operation. The pulse rate before operation in the horizontal position was 92 beats per minute. Other results are given in Tables III and IV and in Figs. 2 and 3.

Subclass 6. Bilateral ventral rhizotomy from the sixth thoracic to the twelfth thoracic, inclusive. Two patients underwent this operation. Their ages were thirty-five and thirty-eight years, respectively. Both had essential hypertension of Wagener's Group IV. The average systolic blood pressure in the horizontal position before operation was 205 mm. of mercury. After operation, the change in blood pressure produced by assumption of the upright position was not as great as before operation although the pressures were definitely lower: 165 mm. in the horizontal position and 153.5 mm. in the upright position. The average diastolic blood pressure in the horizontal position before operation was 122.5 mm. The average pulse rate in the horizontal position before operation was 92 beats per minute. Other results are given in Tables III and IV and in Figs. 2 and 3.

Subclass 7. Bilateral ventral rhizotomy from the sixth thoracic to the second lumbar, inclusive. Seven patients were subjected to this operation. Their ages ranged from twenty-three to forty-five years, with an average age of thirty-four years. All had essential hypertension. Of five, the condition was of Group III (Wagener's classification); of one, Group III plus, and of one, Group IV. The average systolic blood pressure in the horizontal position before operation was 215.7 mm. The decrease in systolic blood pressure caused by voluntary change in posture (horizontal to upright; measurements made after operation only) was

slightly greater than the decrease in systolic blood pressure caused by operation (measurements made in the horizontal position only). The change in blood pressure caused by change of posture (mentioned in the previous sentence) was not nearly so great as the difference between the blood pressure before and after operation (measurements made in the upright position only). The average diastolic blood pressure in the horizontal position before operation was 145.7 mm. of mercury. There was a definite decrease in the diastolic pressure caused by voluntary change in posture (horizontal to upright, measurements made after operation only). The decrease mentioned in the preceding sentence was only half as great as the difference between the diastolic blood pressure before and after operation (measurements made in the upright position only). After operation there was a definite decrease in the diastolic blood pressure but only one-half as great as the difference in the diastolic pressure in the upright position following operation. The average pulse rate in the horizontal position before operation was 87.4 beats per minute. Other results are given in Tables III and IV and in Figs. 2 and 3.

Subclass 8. Bilateral ventral rhizotomy from the fifth thoracic to the second lumbar. Three patients were subjected to this operation. Their ages ranged from twenty-two years to forty-two years, with an average age of thirty-two years. The first patient had essential hypertension, Group II (Wagener's classification) and the other two had essential hypertension, Group III. The average systolic pressure in the horizontal position before operation was 202.6 mm. of mercury. The change in systolic blood pressure caused by operation (measurements made in the same position after, as before, operation) was nearly three times as great as the change in systolic blood pressure caused by voluntary change in posture (horizontal to upright, measurements made after operation only). The average diastolic pressure in the horizontal position before operation was 135 mm. of mercury. The decrease in diastolic blood pressure with voluntary change in posture (horizontal to upright, measurements made after operation only) was not nearly so great as that caused by operation (measurements made in the same position after, as before, operation). The average pulse rate in the horizontal position before operation was 78 beats per minute. Other figures are given in Tables III and IV and Figs. 2 and 3.

Class 8. Patients Subjected to Bilateral Splanchnic Resection, Partial Resection of the Celiac Plexus and Bilateral Partial Resection of the Suprarenal Glands, With Bilateral Removal of the First and the Second Lumbar Ganglions and the Intervening Trunks.—This class was represented by twelve patients who had essential hypertension of varying severity. Their ages ranged from twenty-one to forty-seven years, with

an average age of thirty-three years. Four of them had essential hypertension, of Group II (Wagener's classification), and eight had essential hypertension, Group III. The average systolic blood pressure was 188.5 mm. The change from the horizontal to the upright position following operation produced marked change in the systolic blood pressure in comparison to the decrease with change of posture before operation. The postural change mentioned in the preceding sentence was only one-half as great as the change caused by operation (measurements made in the horizontal position only) and one-third as great as the change caused by operation (measurements made in the upright position only). The average diastolic blood pressure in the horizontal position before operation was 120.9 mm. In the change from the horizontal to the upright position (measurements made after operation only) the decrease in diastolic blood pressure was only one-third as great as the difference between the diastolic pressure before and after operation (measurements made in the upright position only). The average pulse rate before operation was 83.8 beats per minute. Other results are given in Tables III and IV and in Figs. 2 and 3.

COMMENT

The problem of the maintenance of blood pressure is more complicated in man than in animals because of the added factor of gravity consequent to the upright position of man. This implies in man either a mechanism which is more complex or which maintains a more delicate regulatory control over the mass of blood in the body. When a man rises from the horizontal to the upright position, the blood tends to accumulate in parts below the level of the heart and the supply to the brain tends to diminish. Theoretically, this diminution stimulates the vasomotor center which sends out impulses constricting the arterioles generally. The vasoconstrictor action in the splanchnic region is probably most significant and in normal man prevents a fall in blood pressure. If this constriction of the arterioles of the splanchnic region in man is the dominant mechanism in the maintenance of blood pressure in the upright position, interruption of the passage of impulses from the vasomotor center to the splanchnic arterioles should remove some of this control and allow a definite drop in the blood pressure, particularly in the upright position. It should be possible to remove this control by section of the splanchnic nerves.

The splanchnic nerves of animals have been sectioned, but the investigations reported were not comparable to this study because the observations on blood pressure were made under anesthesia in some instances and in all cases in one position, the horizontal one. In the present study the observations of blood pressure and pulse rate were made on human subjects in both the horizontal and the upright positions.

Sufficient time was allowed for the subjects to recover from surgical shock so that the experiments were not acute and were not complicated by anesthesia.

It is interesting to note that in observations of human subjects whose blood pressure was normal, the blood pressure was found to be practically unchanged by various operations, including extensive splanchnic resection. Even in the upright position their blood pressure was the same after operation as before it.

The patients who had essential hypertension and who underwent bilateral, posterior, infradiaphragmatic resection of the splanchnic nerves showed practically the same change in blood pressure when they assumed the upright position following operation as they had shown before operation. Since the splanchnic nerves may show a varied anatomical distribution, the denervation may not have been complete in this operation.

In the cases in which partial ventral rhizotomy was performed, it is evident that unless complete denervation of the splanchnic region was accomplished, no great change in blood pressure took place in the shift from the horizontal to the upright position. After extensive ventral rhizotomy, at least from the seventh thoracic to the second lumbar, inclusive, the effect of posture in decreasing the blood pressure was practically twice as great as before operation. With this operation, section of fibers which formed the splanchnic nerves, along with denervation of the suprarenal glands and paralysis of the muscles of the abdominal wall, were effected. The question might be raised as to the influence of the loss of muscular tone of the abdominal wall. In one case bilateral section of the intercostal nerves from the seventh to the eleventh inclusive was done and caused paralysis of the muscles of the abdominal wall but caused no effect on the blood pressure when the upright position was assumed from the horizontal. This would appear to demonstrate that relaxation of the intercostal and abdominal muscles alone was not sufficient to lower the blood pressure in this instance and that the vasomotor system plays the predominant rôle in the decrease of blood pressure when the upright position is assumed from the horizontal position. Whereas relaxation of the intercostal and abdominal muscles obviously was not a dominant factor in the lowering of the blood pressure in this particular case, it is probably an accessory but minor factor in lowering the blood pressure following extensive rhizotomy. Evidence of this has been obtained by application of a tight abdominal binder which prevented the marked fall in blood pressure as a result of the upright position. Denervation or resection of the suprarenal glands alone apparently has not greatly affected the blood pressure in cases of essential hypertension. In one case of essential hypertension, not referred to

here, but mentioned by Adson, Craig, and Brown in their paper, Walters completely removed one suprarenal gland and removed three-fifths of the other suprarenal gland but produced little effect on the blood pressure.

In the last group of patients on whom bilateral splanchnic resection, partial resection of the celiac plexus and bilateral partial resection of the suprarenal glands with bilateral removal of the first and second lumbar ganglions and the intervening trunks were performed, the results of posture on blood pressure were practically the same as in the cases of extensive ventral rhizotomy. Whereas resection of the lumbar ganglions alone did not cause the blood pressure in the upright position to be less after operation than it had been in the same position before operation, when performed in addition to bilateral resection of the splanchnic nerves, it seemed to furnish by vasodilatation a larger vascular bed with less resistance, thereby helping to lower the blood pressure. Evidence of the importance of lumbar ganglionectomy was given by the effect on the blood pressure of two patients who were subjected to bilateral ventral rhizotomy from the sixth to the twelfth thoracic, inclusive, and by the effect on the blood pressure of the group of patients who underwent ventral rhizotomy from the sixth thoracic to the second lumbar, inclusive. The decrease in blood pressure, with change from the horizontal to the upright position, was three times as great following the latter as following the former operation.

In this study, the similarity between postural hypotension and the results obtained by anterior rhizotomy is evident. Following extensive ventral rhizotomy, the postural effects produced and the loss of sweating were the same as in some cases of postural hypotension.

Operation on the sympathetic nervous system does not cause much change in blood pressure of normal individuals but does cause change in blood pressure of persons who have essential hypertension. The question arises as to the cause of this difference. The etiology of essential hypertension is not definitely known. It has been suggested that it may be either a central abnormality, such as hypersensitivity of the vasomotor center in the diencephalon, or an abnormality of the peripheral mechanism. It is possible that normal blood pressure is maintained automatically without much participation of a central pressor mechanism, whereas increased blood pressure results somewhat from a central pressor mechanism, disconnection of which from the peripheral effectors allows a drop in blood pressure when the patient stands.

It is evident from these studies that significant decreases in blood pressure of patients who have essential hypertension, particularly in the upright position, are not produced by surgical methods except when extensive abdominal sympathetic denervation is effected.

SUMMARY

Before posterior infradiaphragmatic bilateral resection of the splanchnic nerves and bilateral removal of the first lumbar ganglions, voluntary change to the upright from the horizontal position in six patients who had essential hypertension caused an average decrease of 9 mm. in the systolic blood pressure and an average increase of 8.4 mm in the diastolic blood pressure. The cardiac rate increased an average of 11.8 beats per minute. Following operation, assumption of the upright position produced an average decrease of 9.1 mm. in the systolic blood pressure and an average increase of 3.2 mm. in the diastolic blood pressure. The cardiac rate increased an average of 12.3 beats per minute.

Voluntary change from the horizontal to the upright position by twenty-six patients, after ventral rhizotomy, caused varied results according to the extensiveness of denervation. Before operation, assumption of the upright position by one patient caused no change in the systolic blood pressure and an increase of 10 mm. of mercury in the diastolic blood pressure. The heart rate increased 22 beats per minute. This patient was subjected to ventral rhizotomy from the eleventh thoracic to the second lumbar, inclusive. Following operation, assumption of the upright position produced a decrease of 15 mm. in the systolic blood pressure and a decrease of 5 mm. in the diastolic blood pressure. The cardiac rate was unchanged. Before operation, assumption of the upright position by seven patients who had essential hypertension caused an average decrease of 21.4 mm. of mercury in the systolic blood pressure and an average decrease of 3.9 mm. in the diastolic blood pressure. The average cardiac rate was increased 18.9 beats per minute. These patients were subjected to ventral rhizotomy from the sixth thoracic to the second lumbar, inclusive. Following operation, assumption of the upright position produced an average decrease in the systolic blood pressure of 49.8 mm. and an average decrease of 21.9 mm. in the diastolic blood pressure. The heart rate increased an average of 29.6 beats per minute. Rhizotomy between these two levels gave results almost in proportion to the extensiveness of the sympathetic denervation.

Before extensive bilateral splanchnic resection, partial resection of the celiac plexus and bilateral partial resection of the suprarenal glands, with bilateral removal of the first and second lumbar ganglions and the intervening trunks, assumption of the upright position by twelve patients who had essential hypertension produced no change in the systolic blood pressure and an average increase in the diastolic blood pressure of 5.3 mm. The pulse rate increased an average of 12 beats per minute. Following operation, assumption of the upright position produced an average decrease of 21.4 mm. in the systolic blood pressure and an average decrease of 10.5 mm. in the diastolic blood pressure. The pulse rate increased an average of 32.9 beats per minute. In both the group of

cases in which extensive rhizotomy was performed, and in this group, the decrease of 21.4 mm. caused by posture was only about one-third as great as the total decrease caused by a combination of operation and posture. It would seem, therefore, that the lowered blood pressures following these surgical procedures are ascribable one-third to an introduced postural effect and two-thirds to the effects of the operations themselves.

Finally, significant decreases in blood pressure of patients who had essential hypertension, particularly when they were in the upright position, were not produced by surgical methods except when extensive abdominal sympathetic denervation was effected. When less radical operations were performed, the magnitude of the decrease seemed roughly proportional to the extent of the denervation.

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Department of Clinical Reports

ANGINA PECTORIS AT THE AGE OF FOURTEEN ASSOCIATED WITH CONGENITAL RUDIMENTARY RIGHT CORONARY ARTERY AND RUDIMENTARY POSTERIOR CUSP OF MITRAL VALVE

WALTER B. WHITING, M.D.
WICHITA FALLS, TEXAS

CASE HISTORY.—J. F., a white schoolgirl, aged fourteen years, was admitted to the Wichita Falls Clinic-Hospital on Nov. 5, 1936, complaining of attacks of severe precordial pain.

She had had "rheumatism" at the age of six and was confined to bed for a period of two weeks at that time. The knees were stiff and swollen, but no elevation of temperature was recorded. Following this illness, she had noticed slight dyspnea when playing out of doors with other children. Otherwise, except for chickenpox, measles, and whooping cough, she had been well until the time of her present illness.

Present illness began in Dec., 1935. Following exposure to cold she suddenly complained late one afternoon of severe substernal pain radiating up into the neck and into the left arm. The pain ceased spontaneously. Similar attacks occurred every afternoon for the next week, after which they became more frequent and severe. The family physician was called and the patient was put to bed. After a month of rest in bed she began to get up and around the house though attacks continued. Mild attacks were relieved by merely standing erect; severe attacks required morphine.

During the extreme hot weather of the summer of 1936, she began to complain of dyspnea, which gradually became severe. The attacks of pain began to come at very frequent, though irregular, intervals. In the morning and late in the afternoon they would occur every twenty minutes unless morphine was given for relief. During the rest of the day and night they would occur at intervals of one or two hours. The attacks were always induced by excitement or by the slightest exertion.

On Nov. 5, 1936 she was brought to the hospital. Soon after admission she was seen in a typical attack. She suddenly complained of agonizing substernal pain which forced her to stand erect. The pain radiated up into the left side of neck and down the left arm. Just before the attack occurred her blood pressure was 140/0 mm. but during the attack it rose to 230/0 mm. Her heart rate increased from 100 to 130 and numerous extrasystoles appeared.

Physical examination showed an apprehensive, dyspneic, cyanotic girl, fairly well developed, and poorly nourished. There was marked pulsation of the vessels of the neck.

Examination of the heart showed the rate to be 100, with occasional extrasystoles. The apex impulse was heaving and forceful. There was marked enlargement, with the left border in the anterior axillary line in the sixth interspace. A systolic murmur of moderate intensity was heard all over the precordium. Along the left sternal border and at the apex there was a loud blowing diastolic murmur, immediately following the second sound.

The lungs were clear. The liver edge was barely palpable below the right costal margin. There was slight edema of the ankles. There was marked pulsation of all peripheral vessels. Her examination otherwise was negative. Her temperature was normal throughout entire period of hospitalization.

Laboratory Findings.—Urine: acid, specific gravity 1.020, albumin none, sugar none, sediment negative. Renal function tests normal. Blood: Wassermann test negative, hemoglobin 80 per cent, erythrocyte count on repeated examinations—3,950,000 to 4,500,000, leukocyte count on repeated examination 7,900 to 8,600.

X-ray examination of the heart showed the following:

Six-foot films of the chest showed no pulmonary abnormality, but a very large cardiac shadow which appeared to be a generalized hypertrophy without the diagnostic shape of any particular lesion was evident.

The electrocardiogram showed the following: P-waves normal. P-R interval .18 second. There was left axis deviation. T_1 inverted. T_2 and T_3 upright. There were occasional ectopic beats of ventricular origin.

Clinical Diagnosis.—Valvular disease: chronic cardiac; aortic insufficiency; angina pectoris; hypertension.

Treatment.—Immediately following admission to the hospital, the patient was given 1 c.c. of salyrgan intravenously and was digitalized. Dyspnea was completely relieved in twenty-four hours, but typical attacks of angina pectoris continued. Nitroglycerin administered under the tongue gave relief in a very few minutes.

After a few days of rest in bed, the attacks became much less frequent, occurring only from four to eight times in twenty-four hours. Aminophyllin was then given for a period of two weeks without apparent benefit. On December 3 the patient began to sit up in a chair for twenty minutes twice a day. Following this her activity was gradually increased. Attacks of angina were no less frequent until Jan. 4, 1937, after which they occurred only once or twice in twenty-four hours. When free of pain her blood pressure was generally about 160/0 mm. During attacks it rose to between 200 and 220 systolic but the diastolic pressure remained at 0. The patient gained much strength. Her weight increased from 96 to 104 pounds. On February 5 she was discharged greatly improved.

On February 8 she returned complaining of severe abdominal pain of thirty-six hours' duration. Physical signs typical of acute appendicitis were present. Leucocyte count was 21,000. Under morphine, evipal, and novocaine anesthesia the abdomen was opened and a gangrenous appendix was removed. Immediate postoperative condition was excellent. The next day her temperature gradually rose to 108° F. Heart rate increased to 140. She became pale, weak, and delirious. All pain was controlled by morphine. Exitus occurred on the third day following operation. Permission to perform an autopsy was obtained, but examination was limited to the abdomen and heart, and it was requested that all the organs be returned to the body.

PATHOLOGICAL REPORT

The appendix removed Feb. 8, 1937, measured 6 cm. by 7 mm. It was acutely inflamed and covered with exudate. There was pus in the lumen. The walls were densely infiltrated with polymorphonuclear leucocytes and there were many small necrotic areas throughout.

Autopsy Findings.—There were no signs of generalized peritonitis. The appendiceal stump was apparently in good condition. It was surrounded by a localized peritonitis of moderate severity.

The pericardial sac contained about 40 c.c. of straw-colored fluid. The heart was moderately enlarged, weighing 425 grams. The bulk of the heart consisted of a greatly hypertrophied left ventricle, the walls of which measured 19 mm. in thickness. The right ventricle was atrophic, the walls measuring only 3 mm. in thickness. The

pulmonic and tricuspid valves were normal. The aortic ring was markedly dilated. The aortic cusps showed no vegetation and were normal except for a rolled appearance of the edges, due to the dilation of the aortic ring. The mitral valve consisted of a large anterior cusp only. The posterior cusp was practically absent. The left coronary artery appeared to be normal though large. The right coronary artery was rudimentary consisting of a small indentation into which no probe could be pushed. The course of the right coronary artery could not be followed over the surface of the ventricle. The conditions under which the autopsy was performed did not permit injection or dissection of the coronary arteries. There were no areas of infarction.

Microscopic examination of the wall of the right ventricle showed atrophy of the muscle fibers, fatty invasion about the arterioles and replacement fibrosis. Microscopic examination of the left ventricle showed hyperplasia and thickening of the muscle fibers. There was no pathological cellular infiltration of the muscle of either ventricle.

Microscopic examination of sections of the aortic and mitral valve cusps showed no pathology.

Anatomical Diagnosis.—1. Congenital abnormality of the heart: rudimentary posterior cusp of the mitral valve; rudimentary right coronary artery. 2. Appendicitis: acute with abscess. 3. Peritonitis: local.

COMMENT

Angina pectoris in early life is probably not as uncommon as a survey of the literature would indicate. No recent case reports can be found.

Attention is called to the clinical diagnosis of valvular disease, which was based upon the physical findings and the history of "rheumatism" followed by progressively increasing symptoms of heart failure.

Post mortem, no signs of inflammatory reaction could be found on the heart valves or in the heart muscle. A congenital insufficiency of the mitral valve increased the work of the left ventricle, apparently causing the hypertrophy of the muscle. No cause for the insufficiency of the aortic valve could be found other than the greatly dilated aortic ring resulting from the deformity of the heart.

The marked difference in the appearance and size of the ventricles of the heart was accounted for by the inadequate blood supply of the right ventricle and the increased work of the left ventricle.

The poor development of the right coronary artery was apparently congenital in origin although the possibility of a thrombosis with subsequent atrophy sometime after birth cannot be entirely excluded.

The relationship of the hypertension to the other findings is not clear except that it was another load to be carried by the burdened left ventricle.

The anatomical basis for angina pectoris in this case cannot be definitely established. It is probable that the following factors were of greatest importance: A blood supply to the right ventricle which had been inadequate since birth; a blood supply to the left ventricle, which though adequate at first, was rendered inadequate by hypertrophy and by increasing work.

COARCTATION OF THE AORTA (ADULT TYPE); CONGENITAL BICUSPID AORTIC VALVE; SUBACUTE BACTERIAL ENDOCARDITIS

CASE REPORT*

H. F. WECHSLER, M.D., AND EINAR GUSTAFSON, M.D.
NEW YORK, N. Y.

THE following case is reported for several reasons besides its comparative rarity. Our patient illustrated two common complications of this defect which are of clinical importance, namely, the association of coarctation of the aorta with congenital bicuspid aortic valve and the tendency for the malformed valve to become the seat of an infective endocarditis. In addition, a histological examination of serial sections through the subdividing ridge of the bicuspd valve was made to prove its congenital origin.

According to Abbott,[1] the incidence of bicuspid aortic valve in relation to a given number of consecutive autopsies has not been accurately determined but she believes it probably approximates that of Osler's,[2] and of Lewis and Grant's[3] series (1.3 and 1.4 per cent respectively). Coarctation of the aorta of the adult type is of much greater rarity, being found in only 0.006 per cent of a large series of necropsies gathered by Blackford.[4] The frequency with which both defects are associated has been stressed by Hamilton and Abbott.[5] In 200 cases of coarctation of the aorta which they analyzed, a congenital bicuspid valve was present in 51 or 25 per cent. Abbott[1] has collected a total of 67 cases of the combination.

The etiology, pathogenesis, and clinical significance of both congenital defects have been dealt with adequately in the literature, especially by Abbott and by Blackford, and need not be considered here.

CASE REPORT

C. G., white male, aged thirty years, was admitted to the Lenox Hill Hospital, Jan. 10, 1936, complaining of dyspnea, weakness, and palpitation. One year prior to admission, he had suffered from dyspnea and fatigue. These symptoms disappeared after a short period of treatment. Two weeks prior to admission, the above symptoms returned, and in addition, he complained of a dull aching, precordial pain on exertion. He had also suffered from hoarseness and a dry, nonproductive cough for several months.

His previous history was irrelevant except for a hernioplasty performed in 1924 and gonorrhea at the age of twenty years. Syphilis was denied.

Physical examination showed an apprehensive, white male, moderately cyanotic and dyspneic. A "brassy" cough was present.

*From the Medical Service of Dr. Otto M. Schwerdtfeger, Lenox Hill Hospital.

The pupils were slightly irregular but both reacted to light and in accommodation.

There was marked arterial pulsation in the neck and the veins were distended but did not fill from below. A tracheal tug was present. The thyroid gland was not palpable.

The thorax exhibited posteriorly many tortuous pulsating vessels, especially along the vertebral borders of the scapulae and along the lower margins of the ribs. At these sites could be felt a marked systolic thrill and in the posterior interscapular regions, at the level of the third dorsal vertebra, a loud blowing systolic murmur was audible. The internal mammary arteries were not visible. The lungs were resonant throughout. Moist râles were present at both bases.

The heart was moderately enlarged downward and to the left, the apex beat being visible in the sixth intercostal space in the anterior axillary line. Both systolic and diastolic thrills were palpable over the base. A diastolic thrill was also felt at the apex. The aortic sounds were replaced by a harsh, systolic murmur followed by a prolonged, high-pitched diastolic blow which was transmitted downward and to the apex and was best heard at the second left interspace. At the apex, in addition, a loud blowing systolic murmur was audible. The pulse was Corrigan in type, regular, rate 86. The blood pressures in the extremities were as follows: right arm: 160/50; left arm: 190/56; right leg: 108/80; left leg: 104/80. A capillary pulse was present.

The liver and spleen were not palpable. There was an absence of pulsation of the abdominal aorta.

The extremities showed slight cyanosis but no clubbing. There was no edema. The reflexes were physiological.

Laboratory Data.—Blood count on admission: Hemoglobin, 94 per cent (Sahli); red blood count, 4,300,000; white blood count, 10,600; polymorphonuclears, 76 per cent; lymphocytes, 13 per cent; monocytes, 11 per cent.

Urinalyses showed a specific gravity range from 1.008 to 1.029, albumin 1 to 2 plus; and red blood cells on only one occasion, two weeks before death.

Blood and spinal fluid Wassermann tests were negative.

Repeated blood cultures revealed the constant presence of *Streptococcus viridans.*

Electrocardiograms taken on several occasions showed variations in the P-R interval from normal to 0.34 second and widening of the QRS complex to 0.12 second at times. The ventricular complex was slurred in all three leads. The P-wave was notched in Leads I and II and frequently inverted in Lead III.

Roentgenograms of the chest revealed an absence of a prominent aortic knob, dimpling of the descending aorta in the left oblique position, and scalloping of the lower margins of the eighth and ninth ribs.

Course.—The temperature rose on the day after admission and continued elevated until his death. It was remittent in character and its upper level ranged between 102° and 103° F. His course was uneventful, except for the discomfort incident to the fever, until the eighteenth day, when an episode of pain and tenderness in the left upper quadrant occurred. The spleen was not palpable and no friction rub was audible. Later, occasional petechiae in the conjunctivae appeared, and the finger-pads were painful and tender at times. Microscopic hematuria did not occur until the sixtieth day. Late in the course of the disease, the spleen was palpable. He became progressively weaker, more anemic, and then developed signs of congestive failure with orthopnea, right hydrothorax, and tender, palpable liver. He expired on the eighty-fifth day of hospitalization.

AUTOPSY

Anatomical description.—The body was that of a well-developed and well-nourished male. The skin and mucous membranes were slightly jaundiced. One petechial hemorrhage was found inside the left lower lid.

On opening the thorax, the heart was seen to be markedly enlarged to the left with some compression of the lung. The right pleural cavity contained about 100 c.c. of clear, amber fluid. The right lung was removed with ease and weighed 775 gm. The left lung was densely adherent to the parietal pleura and weighed 725 gm. Both lower lobes and the posterior half of the right middle lobe showed scattered areas of consolidation.

The pericardial sac contained about 30 c.c. of slightly turbid, pale yellowish fluid. The heart and aorta weighed 800 gm. (Fig. 1). The right auricle and ven-

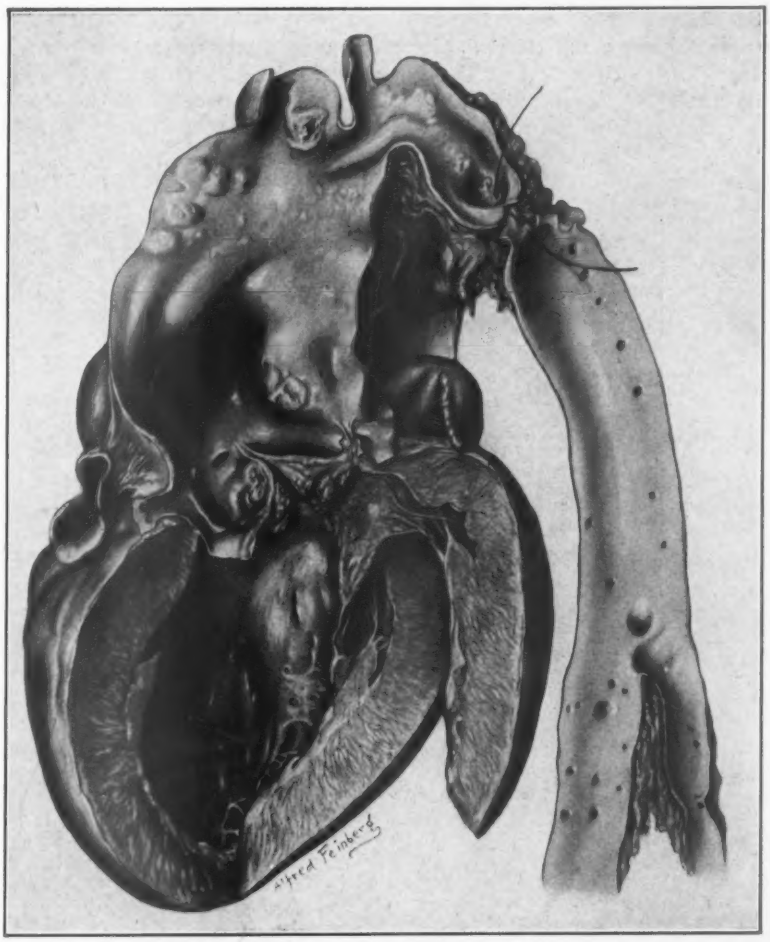

Fig. 1.—Drawing of the left ventricle and aorta showing the bicuspid aortic valve involved by a vegetative endocarditis and the site of the coarctation.

tricle were moderately dilated. The tricuspid valve measured 6 cm. in diameter and the endocardium over the leaflets was smooth and pale gray. The right ventricular wall was 8 mm. thick. The pulmonary valve, artery, and veins showed no gross anatomical lesions. The left ventricle was markedly hypertrophied and dilated and the middle of its anterior wall was 2.6 cm. thick. The papillary muscles were hypertrophied. The mitral valve measured 4 cm. in diameter.

The coronary arteries were dilated and exhibited a few scattered, yellowish, intimal plaques.

The aortic valve exhibited but two complete cusps. One lay posteriorly and somewhat to the right and represented the coronary-free cusp. The other lay anteriorly and slightly to the left. The latter was subdivided at approximately its middle by a shallow ridge. The division of this cusp into right and left anterior cusps was not marked by any indentation on its ventricular surface. Both cusps were partially covered by large friable vegetations. The vegetations almost completely covered the entire length of the coronary-free cusp and extended down on the posterior surface of the aortic cusp of the mitral valve. Only the left half of the other cusp was involved by the vegetations, which had, however, ulcerated through the cusp near its posterior insertion. Where visible the free edges of the cusp were thickened and rounded. Both coronary orifices arose about the level of the origin of the ridge. The left coronary orifice lay approximately in the center of that portion of the sinus of Valsalva between the raphe and the anterior insertion of the double cusp. The right coronary orifice lay close to the insertion of

Fig. 2.—Photomicrograph of a section of the raphe of the bicuspid valve (×15). Weigert's elastic tissue stain.

this cusp, 1.4 cm. from the raphe. The subdividing ridge measured 15 mm. in length, its greatest width located near its center measured 6 mm. and its greatest height measured 5 mm. It was pearly gray and smooth and widened near its insertion to assume a bifid appearance and to fuse with the cusp, 8 mm. below its free edge. There was a small, mottled, yellowish, nodular thickening of the raphe at its origin. The coronary-free cusp measured 3.8 cm. and the double cusp, 4.2 cm. in length.

The aorta rapidly enlarged after its origin to form an aneurysmal dilatation which bulged outward and to the right. Its wall was markedly thinned. Immediately above the valve, the circumference of the aorta was 9.3 cm. and its greatest width at the aneurysm was 13.1 cm. At the level of the innominate arteries, it had narrowed to 4.8 cm., at the left carotid, to 2.1 cm. and at the left subclavian, to 1.8 cm. Beyond the left subclavian there was a sudden narrowing of the aorta to where it terminated at the level of the closed ligamentum arteriosum, 12.6 cm.

above the aortic valve. The descending aorta, 2 cm. below the stricture, had widened to 3.5 cm. The branches from the arch as well as the abdominal branches were dilated. The internal mammary arteries averaged 8 mm. in diameter. Above the anterior commissure and the coronary-free cusp were several raised, yellowish, arteriosclerotic plaques. There were several such plaques about the orifice of the right innominate and in the narrow termination of the aorta.

The parietal and visceral abdominal peritoneum were grossly normal. The liver was enlarged, weighing 1,975 gm. and extended 8 cm. below the costal margin. On section, it was yellowish pink in color and the parenchymal markings were indistinct. The spleen was enlarged to about twice its normal size, weighed 300 gm. and was covered by a smooth, dark bluish capsule. It was soft in consistency. On section, the pulp was softened and congested and the corpuscles were prominent. The kidneys were slightly enlarged, each weighing 200 gm. The capsules stripped with ease and the surface was smooth and congested. On section, the markings were indistinct. The other organs were grossly normal.

The anatomical diagnosis was: hypertrophy and dilatation of the left heart; bicuspid aortic valve; vegetative endocarditis involving the aortic and mitral valves; coarctation of the aorta (adult type); aneurysm of the ascending aorta; moderate arteriosclerosis of the aorta; right hydrothorax; left chronic adhesive pleuritis; bilateral bronchopneumonia; congestion and fatty degeneration of the liver; acute splenic tumor; congestion of the kidneys; petechial hemorrhage in the conjunctiva of the left lower eyelid.

Histological Examination.—Serial sections through the aortic half of the subdividing ridge, including the adjacent portion of the sinuses, were stained with hematoxylin-eosin and Weigert's elastic tissue stain (Fig. 2). These showed the aorta adjacent to the ridge to be composed of the usual three layers. The intima exhibited a rather well-defined internal elastic lamina. The inner two-thirds of the media had an abundance of elastic fibrils arranged in the classic pattern, while the outer third was composed of fibromuscular tissue and contained very few elastic fibrils. As the ridge was approached, the elastic portion of the media became narrowed and condensed. The intima was continued over the ridge, as was the major portion of the condensed layer of the media, both being so fused that a definite subendothelial layer or internal elastic lamina could not be distinguished. The rest of the condensed layer was broken up and lost in the fibromuscular tissue at the base of the raphe. The body of the ridge was composed of irregular whorls of hyaline, fibrous tissue which was continuous with the outer third of the medial coat. Small collections of elastic tissue fragments were present near the surface of the ridge.

Sections through the aorta showed a moderate fibrosis of the media. In the floor of the aneurysmal dilatation it was markedly thinned.

The heart muscle showed occasional small collections of leucocytes and moderate congestion. The lungs showed congestion, edema, and bronchopneumonia. The liver was congested and exhibited marked fatty degeneration. The spleen was deeply congested. The glomerular tufts of the kidneys were swollen and some were partially adherent to the capsule. A moderate tubular degeneration was present.

COMMENT

The case here reported is a typical example of coarctation of the aorta of the adult type exhibiting the classical clinical and roentgenographic findings which made possible a diagnosis during life. Its clinical importance does not end here as it illustrates the fact that a diagnosis of an associated congenital bicuspid aortic valve could also have been made with a great degree of certainty. The frequency

of its combination with coarctation of the aorta has already been alluded to. The tendency of the malformed valve to undergo a chronic sclerotic process with resultant thickening, calcification, and deformity and the predilection for this chronic lesion to become the seat of acute or subacute infectious endocarditis are well known. Lewis and Grant[3] have shown that subacute bacterial endocarditis is the cause of death in a great majority of the cases of bicuspid aortic valve. The occurrence, therefore, of a subacute bacterial endocarditis involving the aortic valve in a case of coarctation of the aorta, should make it highly presumptive that a bicuspid aortic valve is also present.

The absence of embolic phenomena in the abdominal viscera and the lower extremities is of interest and is easily explained by the anatomical conditions present.

Pathologically, the bicuspid valve conforms in every way to the macroscopic criteria for a congenital bicuspid valve as first formulated by Osler[2] and then by Lewis and Grant[3] and to the distinctive microscopic features as described by the latter. The microscopic criteria are naturally more important, as the frequency of superimposed degenerative or infective processes on the valve make the differentiation between those of congenital origin and those due to postnatal inflammatory fusion extremely difficult on gross appearance only.

The aneurysmal dilatation of the aorta is the usual concomitant of coarctation and is a common cause of death.

SUMMARY

A case of coarctation of the aorta is presented which was associated with a congenital bicuspid aortic valve on which was superimposed a subacute bacterial endocarditis. A histologic examination of the raphe of the malformed cusp is included.

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ANEURYSM OF THE ARCH OF THE AORTA DUE TO PERSISTENCE OF A PORTION OF THE DUCTUS ARTERIOSUS IN AN ADULT*

MARK D. ALTSCHULE, M.D.
BOSTON, MASS.

INCOMPLETE closure of the ductus arteriosus is not an uncommon post-mortem finding in infants who die during the first weeks of life. Persistence of only a portion of the duct of Botalli in adults, however, is exceedingly rare; the only previously reported case available in the literature is that of Hebb.[1]

REPORT OF CASE

J. O. (Hospital No. 74509, Med. No. 39173), a fifty-six-year-old married Scotch upholsterer, with an irrelevant past history, entered the Peter Bent Brigham Hospital for the second time on Feb. 3, 1932, complaining of increasingly severe dyspnea on exertion of three and one-half years' duration. He had also had a severe dry hacking cough, orthopnea, and slight swelling of the ankles beginning in June, 1931, requiring admission to the hospital at that time. Hospitalization resulted in only temporary improvement. Physical examinations at the time of both admissions to the hospital were essentially the same, the principal physical findings consisting of respiratory difficulty, cyanosis, enlargement of the heart to percussion, a harsh apical systolic murmur, auricular fibrillation, numerous râles in both lungs, slight enlargement of the liver, and slight edema of the ankles. The blood pressure was 230 mm. of mercury systolic and 140 mm. of mercury diastolic. Ophthalmoscopic examination revealed absence of disc margins and physiological cupping, and the presence of marked vascular changes and many patches of hemorrhage and exudate in both eyegrounds. During the two weeks of his second hospital stay he had repeated attacks of fever, slight jaundice, tachycardia, and exacerbation of dyspnea. He died suddenly on Feb. 19, 1932.

Autopsy (No. A32-19) was performed ten hours post mortem.

A cone-shaped sacculation, measuring 1 cm. in diameter at its base and 1 cm. in depth, was found springing from the wall of the aorta at the point at which it crossed the pulmonary artery. The apex of the cone pointed toward the pulmonary artery, and was connected with it by a fibrous cord 1 cm. long. The attachment of the fibrous cord was marked by a dimple 2 mm. in diameter in the intima of the pulmonary artery. A mottled greyish yellow, granular, adherent thrombus filled the sacculation and extended 3 mm. beyond its orifice. On microscopic examination of the aneurysm, capillaries and young fibroblasts were seen growing into the base of the thrombus from the much thickened subjacent intima. Endothelium was growing from the adjacent portion of the intima of the aorta over the top of the thrombus at its edges. The cord running from the aneurysm to the pulmonary artery was found to consist of dense collagen containing a few clusters of round cells. The intima of the pulmonary artery was thickened at the point of attachment of the fibrous cord, with which it was continuous. Paralleling this fibrous cord were small bundles of smooth muscle.

The heart weighed 550 grams; the thickness of the wall of the left ventricle was 14 to 16 mm. and that of the right, 2 to 4 mm. A mural thrombus filled the left auricular appendage; another was situated on the posterior wall of the left auricle, and a third, 1 cm. in diameter, overlay an area of recent infarction of the same

*From the Pathological Laboratory, Peter Bent Brigham Hospital.

size in the apex of the right ventricle. The left lung contained twelve areas of recent hemorrhagic infarction. The other important findings consisted of moderate generalized arteriosclerosis, moderate arteriolar medial hyalinization and hypertrophy in the heart, brain, and all the abdominal viscera, marked congestion of all the organs, marked central necrosis of the liver, small areas of hemorrhage in the brain, pancreas, and bladder, slight vascular nephritis, chronic cholecystitis, and evidence of a small amount of acute and chronic inflammation of the pancreas. One medium-sized artery in the pancreas was filled with an organizing thrombus.

DISCUSSION

Complete patency of the ductus arteriosus is a congenital anomaly not uncommonly found in adults. Incomplete closure of the ductus in an adult, however, has heretofore been noted only once. The only

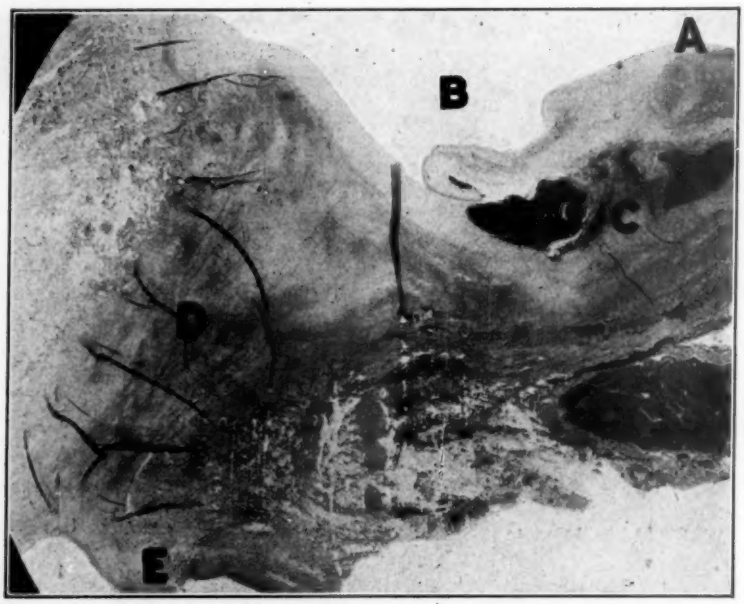

Fig. 1.—Section through the incompletely closed ductus arteriosus. *A.* Aorta. *B.* Aneurysm. *C.* Thrombus. *D.* Obliterated portion of ductus arteriosus. *E.* Pulmonary artery.

other case in the literature, that described by Hebb,[1] was a man of forty years of age who died of pulmonary tuberculosis. In him the patent portion of the ductus was described as follows: "Just beyond and opposite the subclavian is a circular aperature ⅛ inch across leading into a spheroidal aneurysm about the size of a walnut. It was entirely filled with firm laminated clot." This structure abutted against the pulmonary artery and the left bronchus. Other congenital anomalies were also found post mortem in Hebb's case; these consisted of complete obliteration of the left branch of pulmonary artery and marked stenosis at its origin of the right.

The reason for partial persistence of the ductus arteriosus in adults cannot be stated. It is possible that the findings in such cases repre-

sent a stage in a very much delayed process of closure. It is to be noted that in Hebb's case, as well as in the one here reported, an increased pulmonary arterial pressure existed, due in the former to marked pulmonic stenosis and in the latter to severe left ventricular failure. Possibly the gradual increase in pulmonary arterial pressure which occurred in both cases finally became sufficient to retard the flow of blood through a patent ductus from the aorta, thereby favoring closure.

In Hebb's case, as well as in the one here reported, the persistent portion of the ductus existed as a small, thrombosed, saccular aneurysm springing from the wall of the aorta. The presence of this anomaly in both cases was entirely unsuspected during life. Its presence cannot be diagnosed since it gives rise to no specific signs or symptoms. It is conceivable, however, that such an aneurysm might become clinically important should a portion of its thrombus become dislodged and give rise to peripheral embolic manifestations. The possible relation of the thrombus in the small pancreatic artery to the thrombus in the persistent portion of the ductus arteriosus in the case here reported should be noted.

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Department of Reviews and Abstracts

Selected Abstracts

Graybiel, Ashton, and White, Paul D.: Diseases of the Heart. A Review of Some Contributions Made During 1936. Arch. Int. Med. 59: 892, 1937.

This annual review of the literature pertaining to diseases of the heart discusses briefly and clearly the important contributions made during the year 1936. The value of such a review is considerable and should be included in one's reading on this subject. Special attention has been given this year to foreign medical reports.

H. McC.

Gross, Louis, Blum, Lester, and Silverman, Gertrude: Experimental Attempts to Increase the Blood Supply to the Dog's Heart by Means of Coronary Sinus Occlusion. J. Exper. Med. 65: 91, 1937.

Sudden occlusion of the left anterior descending branch approximately 2 cm. below the ostium of the left circumflex coronary artery in the dog's heart produces a mortality rate of approximately 50 per cent. In dogs weighing approximately 15 kilograms surviving more than twenty-four hours (average one week), an infarction is produced which almost invariably measures 5 by 5 cm. on surface. Following coronary sinus obturation, such secondary sudden occlusion of the left anterior descending branch is followed either by no infarction or by a reduction in the size of the infarct. The success of the procedure, quite apart from the mortality rate, depends upon the completeness of the coronary sinus obturation. On the other hand, sudden and complete coronary sinus obturation by itself is associated with a high operative mortality and apparently does not affect the mortality rate following subsequent sudden left anterior descending branch occlusion. Partial persistent obturation of the coronary sinus, however, is in itself associated with a low operative mortality. Furthermore, its experimental production in dogs appears to lower the mortality rate following subsequent sudden occlusion of the left anterior descending branch and to diminish the extent of the infarction.

In the introduction to this report it was pointed out that there are three important desiderata to the problem of improving the coronary circulation in the human heart. The findings herein reported fulfill these requisites to an encouraging degree. It has been shown that, following the outlined procedures, a functional increase in the blood supply to the heart can be produced in a significant proportion of experimental animals, this varying with the nature of the experimental procedure. The manipulation is simple, can be performed in the dog within approximately twenty minutes, and does not lead to appreciable pericardial adhesions. Increase in the nutrition of the myocardium is noted one week after the experimental procedure. Although no experiments employing sudden left anterior descending coronary branch occlusion were carried out sooner than one week, there is available anatomical evidence that within possibly twenty-four hours after coronary sinus occlusion a dilatation of the vascular bed occurs. In subsequent experiments attempts will be made to determine whether this early vascular dilatation is adequate to compensate for subsequent sudden left anterior descending branch occlusion.

A discussion is given of the results following various coronary sinus occlusion procedures in which it is indicated that it is desirable to produce a partial or gradual occlusion in order to lower the mortality rate of the initial procedure as well as of the subsequent sudden arterial occlusion. Experiments thus far reported on cardiopexy operations are lacking evidence that they are associated with appreciable improvement in the vascular nutrition of the myocardium.

AUTHOR.

Gross, Louis, Mendlowitz, Milton, and Schauer, Gerhard: Hemodynamics Following Experimental Coronary Occlusion in Dogs. Proc. Soc. Exper. Biol. & Med. **35**: 446, 1936.

Following left anterior descending coronary branch ligation in the open or closed chest, there is an immediate appreciable fall in average cardiac output and also a delay in cyanide circulation time. Control experiments indicate that these changes are directly attributable to the ligation of the coronary branch. Following these procedures, there are no other appreciable changes in the hemodynamics studied.

AUTHOR.

Herbst, R., and Manigold, K.: The Reaction of the Circulation and Respiration in Anoxemia. Arbeitsphysiol. **9**: 166, 1936.

It was found that, when the pressure was reduced to one-half atmosphere in a low pressure chamber, no change in circulation could be demonstrated in normal recumbent persons. With pressures lower than this, the pulse accelerated (approximately as a logarithmic function of the pressure). At low pressures, systolic and pulse pressures rose and an increase in cardiac stroke volume occurred in some instances. At very low pressures collapse occurred, with the pulse slowing and pressures and stroke volume decreasing. Oxygen inhalation quickly relieved the symptoms. Respirations during the lowering of pressure in the chamber became slower and deeper.

L. N. K.

Werle, E., and Hürter, J.: Ornitho-Kallikrein I. Biochem. Ztschr. **285**: 175, 1936.

From the pancreas and other organs of birds (pigeon, hen, and goose) an extract was obtained which lowers the blood pressure in birds but not in mammals (cat and dog). Mammalian *Kallikrein*, which lowers the blood pressure in mammals, has no effect on birds.

L. N. K.

v. Euler, U. S.: Observations on Substance P, the Atropinfast, Intestine Stimulating and Blood Vessel Dilating Substance Obtained From the Intestines and the Brain. Arch. f. exper. Path. u. Pharmakol. **181**: 181, 1936.

This is a continuation of the study of a new substance isolated by Euler and Gaddum. Trypsin inactivates the substance, indicating its albuminose character. It lowers blood pressure and stimulates the gut and uterus. Since it is found in biodialysates of rabbit gut, it presumably plays an important rôle in the movements of the gut normally.

L. N. K.

Klisiecki, A.: The Flow of Blood in the Aortic Arch. Ztschr. f. Biol. 97: 1, 1936.

A modified photohemotachometer of Cybulski's was used in a dog, and, surprisingly, the author found that there is no systolic acceleration of blood flow in the aorta when the vessel is permitted to expand and the rate of the dog's heart is normal. When the pulse rate is slowed, a pulsatory variation in linear velocity of flow occurs during the heart cycle. At very slow rates the velocity varies from 0 mm. rate in diastole to 400 mm. per second in systole.

L. N. K.

Weiss, Soma, and Wilkins, Robert W.: The Nature of the Cardiovascular Disturbances in Vitamin Deficiency States. Tr. A. Am. Physicians, p. 341, 1936.

Dysfunction of the cardiovascular system may develop as the result of an unbalanced food intake, particularly lacking in vitamin B. The condition may affect a normal or a previously diseased heart. The cardiovascular manifestations here described depend partly on changes in the nervous system and partly on changes in the myocardium and the vascular system.

Simple tachycardia, vagus reflex irritability with bradycardia or with asystole and syncope, right-sided and left-sided heart failure, peripheral arteriolar dilatation, and vasomotor collapse with vascular constriction were observed in various combinations.

With rest and a dietary regime the circulatory disturbances disappeared rapidly in one group and slowly in another group. Sudden death as a result of vasomotor collapse also occurred.

In 38 cases the electrocardiograms were normal in but 3 instances. The main abnormalities were changes in the T-waves and low amplitude and prolongation of the electrical systole (Q-T). Under therapeutic measures these changes usually disappeared.

The histological changes in the cardiac muscle and conductive systems were identical with those described by Wenckebach in beriberi heart of Java. These changes, however, are not specific or characteristic of hearts in deficiency diseases.

The coexistence of polyneuritis and the cardiovascular disturbances described serves as additional evidence for the vitamin B deficiency theory of "alcoholic polyneuritis."

Cardiovascular manifestations associated with vitamin B deficiency are more than mere sporadic manifestations in the northeast and probably in other sections of the United States. The condition here described may well bear pertinently on the behavior and the mortality rates of alcoholic and nonalcoholic patients with vitamin B deficiencies (beriberi and pellagra) in the presence of infection, in association with high metabolic rates in general, and under surgical conditions. The therapeutic implications under these conditions are discussed.

AUTHOR.

Parkinson, John, and Hoyle, Clifford: The Heart in Emphysema. Quart. J. Med. 6: 59, 1937.

Eighty patients suffering from a high grade of emphysema were investigated, chiefly in regard to the cardiovascular system and particularly with reference to the size and shape of the heart as judged by radiology.

The cardiac factor in emphysema alone is seldom pronounced except late in the disease, and then not always, unless there is also a cardiac lesion of another sort. A complicated etiology is so common that it was demonstrable in more than half of this series, and the complication was predominantly hypertension. It may be

said that cardiac symptoms and signs in emphysema are more likely to be due to hypertension than to the direct effect of emphysema on the heart.

Clinical evidence is an uncertain guide to involvement of the heart in either pure emphysema or when this is combined with other cardiovascular disease. Cardiac and pulmonary symptoms are similar, and the physical signs in emphysema indicative of a cardiac element are admittedly few. In particular there is no guide to cardiac enlargement, and as this is a proof that the heart is implicated, we are dependent on radiology, except in late examples where edema is proof enough that the heart is involved. Electrocardiographic evidence is disappointing, for there is right ventricular predominance in a small proportion only; its chief value is to provide other evidence of a complicating myocardial (coronary) disease, e.g. a bundle-branch lesion.

The most frequent and radiological change in the cardiac involvement of emphysema is enlargement of the branches of the pulmonary artery at the hila (about 46 per cent). In the anterior view the enlarged pulmonary or middle arc is sometimes obscured by its large left branch. Localized enlargement of the heart is the second main proof that the heart is implicated in emphysema, and it is demonstrable in over one-third (about 40 per cent). It concerns most often the conus pulmonalis of the right ventricle (about 41 per cent), and in about one-half these the body of the right ventricle also, best seen in the left (II) oblique and right (I) oblique positions, respectively. Enlargement of the right auricle is not common (about 14 per cent).

Enlargement of the left ventricle (about 30 per cent) and of the left auricle (about 1 per cent) is dependent upon the coexistence of other cardiovascular disease, for in pure examples of emphysema it does not occur, unless, perhaps, in the late stage of congestive failure. Systemic hypertension is the almost invariable cause of the left ventricular enlargement when this is found; a few others have myocardial (coronary) disease, e.g., with bundle-branch block. Enlargement of the left auricle was found once only, and that in the sole instance of auricular fibrillation. The infrequency of enlargement of the right auricle and the rarity of enlargement of the left auricle can be related to the freedom from auricular fibrillation and to the admitted rarity of failure at all from emphysema alone.

The heart as a whole is not enlarged in uncomplicated cases of emphysema. Great enlargement of the right heart is rare, being seen in four only. In none of these was there a sabot appearance. About one-third of patients have no enlargement at all and no changes in the pulmonary vessels radiologically. The small and droplike heart shadow, though so often held to be characteristic of emphysema, is in our experience only seen occasionally.

These results from the use of x-rays now permit recognition in life of the features of enlargement long known to morbid anatomists. They go further in that most of these traditional records are largely diminished in value by the inclusion of unrecognized associated hypertension or myocardial disease. In pure emphysema it is the outflow tract of the right ventricle (Kirsch) extending from the apex to the pulmonary artery, which is earliest affected by enlargement and manifested by prominence of the conus. Later the body of the right ventricle is also involved, and this is represented by right ventricular prominence in the left (II) oblique position. These are the changes in the heart characteristic of pulmonary hypertension. Cardiac failure from emphysema alone is surprisingly rare; and, when it occurs, it is with normal rhythm and edema, and as a very late event that is almost invariably terminal. Recurrent attacks of failure are almost unknown. Examples of failure apparently due to emphysema are most often explained by associated cardiovascular disease, usually hypertension, and in such, failure can be recurrent. The differential diagnosis, especially from mitral stenosis, congenital heart disease, and the heart in patients with goiter, is briefly discussed.

AUTHOR.

Van Nieuwenhuizen, C. L. C., and Hartog, H. A. P.: Chest Leads in Electrocardiography. Arch. Int. Med. **59**: 448, 1937.

Data obtained from the chest lead derived as a routine method are discussed on a basis of 1,500 tracings. In coronary thrombosis the chest lead often offers the only electrocardiographic diagnostic evidence. The importance of the chest lead for the differential diagnosis of acute intrathoracic or abdominal deviations with coronary thrombosis is pointed out. The chest lead may be of much value also in reaching a diagnosis in a case of gradually arising myocardial infarction. The tracings obtained in coronary thrombosis are divided into two groups, one of which was caused by anterior infarction and the other possibly by posterior or septal infarction.

It is not improbable that these last curves indicated an atypical bundle-branch block. But there still remains the question whether the cause is not an insufficiency of the blood supply by the posterior coronary artery. The latter form of tracing was seen in one case of rheumatic myocarditis. The history of a patient in the first group usually records an acute attack; that of a patient in the second group usually bears no record of a sudden attack of pain or oppression. This is the reason these myocardial changes often escape clinical observation. Next the clinical significance of an abnormally deep T-wave (deeper than –10 mm.) is pointed out. With a few exceptions such a wave is always found in organic disease of the heart. In cases of mitral stenosis, however, the T-waves in the standard leads are strongly positive; in other groups (hypertension, chronic nephritis, and aortic defects) all or part of them are abnormal. The hypothesis is advanced that the deep T-wave in mitral stenosis is the result of a difference in the position of the heart; in the other groups this might be the result of myocardial disease. A deep T-wave is found also in bundle-branch block. Then, however, the ventricular complex is very high and large, in analogy to the diphasic ventricular complexes in the other leads.

Finally the importance of the chest lead in making an electrocardiographic diagnosis of diffuse myocardial damage is demonstrated either as a support for the third lead or as the sole criterion. Here the T-wave may be shallow, diphasic, or positive. Other factors which influence the shape of the T-wave in the chest lead are digitalis and a longitudinal position of the heart, especially in children.

AUTHOR.

Ludwig, H., and Bener, A.: Audible Auricular Sounds in Auricular Flutter. Klin. Wchnschr. **15**: 271, 1936.

A case of flutter of the auricles is reported in which each auricular contraction is accompanied by an audible sound, best heard in the second and third intercostal spaces in the left parasternal line. This was recorded photographically. The flutter rate was 250 per minute. There was total and later irregular A-V block and also intraventricular block. The heart was large, and there was cardiac failure. A loud systolic murmur was present at the apex, and a loud diastolic murmur was heard over the lower sternum.

L. N. K.

Feil, Harold: Preliminary Pain in Coronary Thrombosis. Am. J. M. Sc. **193**: 42, 1937.

Fifteen cases of coronary thrombosis, with myocardial infarction in fourteen, have been observed with preliminary mild anginal attacks preceding the clinical picture of thrombosis by hours or days—usually from twelve to forty-eight hours. This pain is not dependent on effort or emotion, is more or less continuous, and is of an oppressive and burning character. The electrocardiogram was normal in two of five patients whose records were taken during this preliminary pain. The abnormal changes in the other cases are described. A gradually forming thrombus in a

stenosed coronary artery appears to be the most probable explanation for the occurrence of the preliminary pain. The possibility of the development of a coronary artery thrombus should be suspected in patients who have persistent retrosternal pain, not related to effort, emotion or digestion, especially when hypertension or the anginal syndrome has been previously noted. Effort should be made to improve coronary artery flow. Urging of fluids (to avoid dehydration), administration of aminophyllin, alcohol, and nitrites, moderate restriction of physical activity, mental rest, and restriction of insulin and tobacco are indicated.

AUTHOR.

Kisch, F.: Statistical Observations on Life Expectancy in Coronary Thrombosis. Klin. Wchnschr. 15: 440, 1936.

The circulatory collapse after coronary thrombosis was followed by death in 23.5 per cent of the cases, the mortality being higher in women than in men. In many cases of coronary thrombosis, the blood sedimentation time may be of prognostic value in determining the progress of the infarct. A characteristic electrocardiographic deviation is compatible with several years of life.

L. N. K.

Thompson, William Paul, and Levine, Samuel A.: Note on the Duration of Symptoms and Age at Death in Chronic Rheumatic Valvular Disease, Especially in Tricuspid Stenosis. Am. J. M. Sc. 193: 4, 1937.

The authors have found that patients with tricuspid stenosis, in spite of the fact that death occurs at a comparatively early age, are able to tolerate their symptoms considerably longer than are those patients in whom the tricuspid valve is not involved. The average figures are, therefore, somewhat paradoxical and contrary to what one might expect. We have attempted to point out, however, that in tricuspid stenosis the symptoms and signs are not due wholly to myocardial failure and that they are due in part to mechanical obstruction to the normal diastolic filling of the heart, so that this apparent paradox is in part, at least, explained.

It is believed that these figures contribute two important clues to the diagnosis of tricuspid stenosis: first, the appearance of symptoms at an early age in patients with chronic rheumatic valvular disease and, second, an ability to carry on with such symptoms for an unusually long time, particularly when the prominent features are enlargement of the liver and ascites. If these features cause us to suspect tricuspid stenosis, we are then one step nearer the goal of making accurate antemortem diagnoses.

AUTHOR.

Reichel, H.: Bacterial Cultures From the Blood in Endocarditis Lenta. Klin. Wchnschr. 15: 642, 1936.

In some cases of endocarditis lenta liquid media are required to demonstrate positive blood cultures. With proper precautions growth will occur in ordinary nutrient broth and macroscopic colonies will appear.

L. N. K.

Cushing, E. H.: Diverticulum of the Pericardium. Arch. Int. Med. 59: 56, 1937.

Thirty-nine cases of diverticulum of the pericardium have been described in the literature, and one additional case is reported here.

This case is the first described in which a pericardial diverticulum has presented on the anterior wall of the chest. The diagnosis was confirmed by injecting air

into the subcutaneous mass and finding air within the pericardial cavity. The roentgenographic findings were typical of those in the cases described by Kienbock and Weiss and by Jansson. The diagnosis of calcified tuberculous pericarditis was confirmed by the demonstration of tubercle bacilli in the pericardial fluid obtained by aspirating the diverticulum and by the death with tuberculosis of guinea pigs inoculated with the fluid.

AUTHOR.

Gross, Louis: So-Called Congenital Bicuspid Aortic Valve. Arch. Path. 23: 350, 1937.

A description is given of the bicuspid aortic valve as observed in sixteen adult hearts, eight of which presented the classic macroscopic criteria described by Osler as indicating congenital origin of the malformation and eight of which failed in one respect or another to fulfil these criteria. These hearts presented no associated developmental abnormalities in this respect, resembling previously described adult hearts with so-called congenital bicuspid aortic valves. Strategic cardiac sites and serial sections of the commissures were examined microscopically. Faulty inversion of the commissure as described by Lewis and Grant was found in only two of the sixteen hearts. It was shown that in the majority, apart from the obvious secondary lesions (bacterial endocarditis, syphilis) and degenerative disease (calcific sclerosis of the aortic valve—Mönckeberg type), there were stigmas which strongly implied an associated, generally extinct, rheumatic process. Evidence is presented which supports the hypothesis that a degenerative process (Mönckeberg type) in the minority of instances and a rheumatic process in the majority of instances lead to the formation of the so-called congenital bicuspid aortic valve in the adult. The pathogenesis of the lesion on a rheumatic basis is described, and attention is drawn to the compatibility of this view with the predisposition of the valve with this deformity to subacute bacterial endocarditis. A discussion of the findings leads to the conclusion that Osler's macroscopic criteria are inadequate and do not necessarily indicate a congenital lesion. Attention is directed to the conspicuous differences between bicuspid aortic valves occurring in children and those found in adults. It is suggested that the microscopic criteria offered by Lewis and Grant for the establishment of such a lesion as congenital should be verified by study of serial sections in a representative number of cases in which the bicuspid condition of the aortic valve is of indisputably congenital developmental origin. Such a condition appears to occur considerably more frequently in infants than in adults and is invariably or almost invariably associated with other developmental cardiac defects. For these reasons it is suggested further that a bicuspid aortic valve occurring in an adult should be considered as congenital only when associated with other congenital malformations of the heart. A bicuspid aortic valve not so associated found in adult life should be designated merely "bicuspid valve."

AUTHOR.

McBroom, Josephine, Sunderland, Douglas A., Mote, John R., and Jones, T. Duckett: Effect of Acute Scurvy on the Guinea-Pig Heart. Arch. Path. 23: 20, 1937.

Acute scurvy in the guinea pig produces degenerative changes in the cardiac valves and myocardium as well as definite proliferative lesions along the line of closure of the valves. These lesions are equally prevalent and severe in total scurvy whether or not there is superimposed infection.

A deficiency of vitamin C, as shown by Wolbach and Howe and by Wolbach, prevents the adequate formation and maintenance of intercellular substance. It may be expected, therefore, that in regions of strain and stress degenerative lesions may occur and that a proliferative reaction may take place in an attempt at repair. It is as such that the lesions produced in the present study are interpreted.

The complete gross and microscopic pathological changes of rheumatic fever are obviously dissimilar from those of scurvy, even though in some of the microscopic lesions of the valves in both conditions there are certain points in common: a subendothelial proliferative reaction with a cellular infiltration and a collagen change. There is also damage to the vascular system in both conditions, but the identity of this injury has not been demonstrated. Although scurvy may indirectly be a factor in lowering the general resistance of the body to infection, there is as yet no evidence that rheumatic fever and scurvy are the same disease, or that there is a direct causal relationship between the two, even with infection by the hemolytic streptococcus complicating the latter. The lesions in the guinea pig heart described by Rinehart and Mettier may be produced by acute scurvy alone and may be interpreted as an attempt at repair of lesions caused by physiological stress on a tissue weakened by acute scorbutus.

AUTHOR.

Bourne, Geoffrey: Acute Rheumatic Meningitis. Brit. M. J. 2: 1017, 1936.

A case of acute rheumatic meningitis is described. A man aged thirty-four years was admitted because of severe rheumatic fever in characteristic form. He developed pericarditis with extensive myocardial injury. After about two weeks there were meningeal signs, and the spinal fluid showed increased pressure with 78 cells. He made an uninterrupted but slow recovery. The central nervous system signs disappeared within about ten days, but the pulse due to the heart block remained for four or five weeks.

It is suggested that for the development of acute meningitis during acute rheumatism some secondary factor such as alcoholism is necessary.

AUTHOR.

Nemet, Geza, and Rosenblatt, Milton B.: Cardiac Failure Secondary to Chronic Pulmonary Tuberculosis. Am. Rev. Tuberc. 35: 713, 1937.

A study of the 71 patients who came to necropsy on the Tuberculosis Division of the Montefiore Hospital during a period of one year revealed 33 instances (46.5 per cent) of right ventricular hypertrophy.

None of the 33 cases was associated with any significant coronary artery disease, valvular disease, or hypertension. There was one instance of antecedent hypertension in a patient with hypertrophy of both ventricles.

Despite enlargement of the right ventricle, the hearts, in general, were smaller than normal.

The duration of the pulmonary disease in these patients did not differ from that seen in all types of tuberculosis patients. All the cases had extensive bilateral involvement and one-third showed definite hematogenous lesions.

Recapitulation of the most significant symptoms revealed the occurrence of dyspnea 30 times (90.9 per cent); cyanosis 23 times (69.6 per cent); hepatomegaly 14 times (42.4 per cent); and peripheral edema 15 times (45.4 per cent). Inconsistencies between the degree of venous distention and venous pressure were noted.

There were too few electrocardiographic studies from which to draw any conclusions. However, review of the literature reveals that right axis deviation with inversion of the T-wave in the second and third leads may be considered indicative of right ventricular enlargement.

Eleven of the 33 cases (33.3 per cent) were recognized during life as having heart disease; in the remaining 22 (66.7 per cent) the diagnosis was entirely post mortem.

It is felt that the inability to distinguish clinically between pulmonary insufficiency and cardiac insufficiency was largely responsible for the low percentage of diagnoses. Dyspnea, cyanosis, venous distention, hepatomegaly, and even edema may be attributable to causes other than cardiac failure in the patient with chronic pulmonary tuberculosis.

The duration of life after cardiac failure had occurred was relatively brief and depended considerably upon the character of the underlying pulmonary process.

The cardinal sign of right ventricular failure is enlargement on fluoroscopy or on the x-ray film. Demonstration of this sign will be facilitated, especially in the early stages, by detailed and frequent studies.

AUTHOR.

Hâban, G.: Aneurysms of All Three Sinuses of Valsalva. Ztschr. f. Kreislaufforsch. **29**: 74, 1937.

In the case reported there was evidence post mortem of syphilitic involvement of the valves. The author, however, believes that a congenital structural weakness played a subsidiary rôle in aiding the syphilis to produce the changes.

L. N. K.

Fuchs, F.: Effect of Denervating the Kidney on Blood Pressure. Wien. klin. Wchnschr. **49**: 495, 1936.

This is a theoretical presentation of unsubstantiated facts purporting to show why denervation of the kidney causes a drop in blood pressure.

L. N. K.

Lutterloh, Charles H.: The Clinical Significance of the Effects of Posture on Blood-Pressure. The Postural Test as a Means of Classifying Hypotension. Am. J. M. Sc. **193**: 87, 1937.

There is presented a study of the effects of posture on the blood pressure and pulse rate in normal adults, normal children, and a group of hypotensive individuals as secondary, essential, and primary hypotension.

The response in the normal groups to postural change from the horizontal to the upright position was a slight fall in the systolic blood pressure, a definite rise in the diastolic blood pressure and a rise in the pulse rate. In the secondary and essential hypotension groups a similar response was noted. The primary hypotension group, however, responded abnormally by manifesting a decided fall in both the systolic and diastolic blood pressures with only a slight increase in the pulse rate.

The similarity between primary hypotension and "postural hypotension" is suggested.

A test for circulatory efficiency and vasomotor stability has been outlined, and as a result of this test a classification of hypotension is presented.

AUTHOR.

Brown, J. J. Mason: Intermittent Venous Occlusion in the Treatment of Obliterative Vascular Disease. Brit. M. J. **1**: 1106, 1937.

Various forms of apparatus for the application of intermittent venous occlusion are described.

Treatment with such apparatus has resulted in the relief of symptoms, healing of ulcerated and gangrenous areas, and increased oscillometric and surface temperature readings.

AUTHOR.

Clara, M.: Arteriovenous Anastomoses. München. med. Wchnschr. **83**: 651, 1936.

The author summarizes the well-known functions of these important anastomoses. These anastomoses are not only important in regulating blood flow locally but influence as well the rate of flow of the entire body. When they open, the rate is increased; when they close, the rate is decreased. In addition, when these anastomoses open, the venous blood becomes arterialized, a centripetal pulse is transmitted from the arteries to the veins and the temperature of the region is elevated.

L. N. K.

Craig, Winchell McK., and Knepper, Paul A.: Cervical Rib and the Scalenus Anticus Syndrome. Ann. Surg. **105**: 556, 1937.

The clinical picture of cervical ribs and that of the scalenus anticus syndrome are very similar, as are also the surgical indications and operation. The symptoms result from compression or irritation of the brachial plexus and compression of the subclavian artery. Compression may be due to the presence of cervical rib, an abnormally low position of the shoulder, high fixation of the sternum and ribs, low origin of the brachial plexus, or elevation of the first thoracic rib from spasm of the scalene muscles brought about by irritation of the brachial plexus. When cervical ribs cannot be demonstrated, resection of the scalenus anticus muscle is usually all that is necessary to relieve the symptoms. In the presence of a cervical rib without tendinous attachments and without obvious pressure from behind, resection of the scalenus anticus muscle is all that is necessary, but when there is evident pressure from the cervical rib or its tendinous attachment, resection of the rib and the attachment should be carried out.

In carefully selected cases in which the symptoms point clearly to either cervical rib or the scalenus anticus syndrome, the surgical result is usually excellent. Six cases are presented to illustrate the points in differential diagnosis, surgical indications, and results.

E. A. H.

Beiglböck, W., and Junk, H.: Muscle Tone and Its Relation to the Peripheral Circulation. Ztschr. f. klin. Med. **131**: 241, 1937.

The method of Henderson, Oughterson, Greenberg, and Searle for measuring intramuscular pressure has been used to study a variety of conditions. The authors agree that the return flow of blood to the heart is in part dependent upon muscle tone, but cite the observation that muscle pressure is not increased in congestive failure with increase in venous pressure as evidence that intra- and extravascular pressures are independent of each other.

The average normal intramuscular pressure in their series of 28 individuals was 76 mm. water. It would have been higher except that several individuals above the age of seventy years were included. All of these had low pressures. They confirm the observations of Henderson, Oughterson, and others, that carbon dioxide and strychnine increase muscular pressure and add that sympathol also does. Histamine decreased it; caffeine, coramine, and cardiazol had no effect. Operation and most febrile diseases lower it. The most well-marked drops were seen in pneumonia.

J. M. S.

Heckmann, K.: The Significance of the Double Summit in the Waves of the Shadowkymogram. Klin. Wchnschr. **15**: 644, 1936.

This double summit in the roentgenkymograph is due occasionally to a cardiac infarct. The author found one instance of right-sided bundle-branch block with this phenomenon. It occurs also in pericardial effusion. It is found without any of these abnormalities and is explained as a systolic displacement of the heart to the left as the aorta lengthens. This causes the second wave, the first being due to systolic contraction.

L. N. K.

Faulkner, James M.: The Treatment of Cardiovascular Emergencies. New England J. Med. **216**: 747, 1937.

The main body of the paper is concerned with cardiac emergencies, but it ends with a capable reminder about diagnosis and treatment of peripheral vascular collapse or shock. Medically, this condition is frequently unrecognized, yet is as common as cardiac collapse, and demands accurate diagnosis in order that its own peculiar therapy can be applied. The clinical picture is the same as that of surgical shock—prostration, pallor, sweating, pinched features, cold extremities, weak heart sounds, rapid thready pulse, and low blood pressure. There is a disparity between the circulating blood volume and the functioning capacity of the vascular bed. The treatment consists, therefore, in increasing the blood volume or in decreasing the capacity of the vascular bed. The former is the more certain procedure and is effected by the same measures as those used in surgical shock. The latter is effected, to some degree, by the use of central nervous system stimulants: caffeine, strychnine, and various camphor derivatives. Digitalis is of no value, and adrenalin is contraindicated.

H. M.

Starr, Isaac: Carbaminoylcholine (Doryl or Lentin): Its Action on Normal Persons in Peripheral Vascular Disease, and in Certain Other Clinical Conditions. Am. J. M. Sc. **193**: 393, 1937.

Carbaminoylcholine chloride is one of the most powerful drugs known. Studies have been conducted on its action after subcutaneous and oral administration to 26 normal volunteers and to a larger number of patients. Special studies of its effect on the heart and circulation have been made in a small group of cases.

The information now at hand concerning its dosage, action, and untoward effects, is sufficient to warrant its cautious use in those cases that its action seems adapted to benefit. The drug causes striking relief of rest pain in certain cases of peripheral vascular disease.

AUTHOR.

Fraenkel, A.: From Empirical to Experimental Digitalis Therapy. Schweiz. med. Wchnschr. **18**: 434, 1936.

Intravenous strophanthin is, in the author's opinion, the only method of quantitative digitalis therapy. It permits much better constant control of dosage than digitalis. He believes that this is particularly true in cases with marked cardiac edema. In slight edema he advocates the use of a salt-free diet in addition to intravenous strophanthin. In severe edema salyrgan can be used with the strophanthin.

L. N. K.